

INTRACRANIAL TUMORS



MEDIEVAL CRANIOTOMY



MODERN CRANIOTOMY

SECOND EDITION

INTRACRANIAL TUMORS

BY

PERCIVAL BAILEY

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SECOND EDITION, 1948

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1829

DEDICATED
to
THREE DEVOTED WOMEN

~

my mother
STELLA ORR BAILEY

my teacher
MARTHA BUCK

my wife
YEVNIGE BASHBAZIRGHANIAN

He who cares for patients suffering from brain-tumour must bring to his problem much thought and stout action. There is need also of a formidable optimism for the dice of the gods are loaded!

FOSTER KENNEDY

PREFACE TO THE SECOND EDITION

Continued demand for this book has necessitated a second edition. Its main thesis remains unchanged but errors have been corrected and recent advances in our knowledge inserted. A brief atlas of roentgen photographs, some of which have already been used in the German translation, has also been added.

The book continues to present its subject from the pathological standpoint. Most discussions of intracranial tumors in the past have been based essentially on regional physiology, with only a perfunctory preliminary chapter on pathology. That orientation was doubtless largely due to the importance and difficulty of the problem of localizing the tumor. Now that it has been solved by increase of our knowledge, and introduction of the method of ventriculography, interest has turned to the possibility of establishing the pathological nature of the growth before operation. In the first edition of this book there was detailed at great length the inadequate resources at our disposal at that time for solving the latter problem. Since then Moniz has introduced the method of arteriography, comparable in its usefulness to ventriculography, by means of which the pathological diagnosis has been greatly facilitated.

Although the emphasis is placed on pathology, regional physiology has not been neglected; in fact some matters which are best observed in cases of intracranial tumor, such as disturbances of function of the hypothalamus and cerebellum, have been treated at length, the more so because they are still often inadequately or even erroneously presented in textbooks available to students.

Some surprise has been expressed that a small field of neurology should be presented to students at such length. Aside from its essential interest, there is another important reason for doing so. Neurology has long suffered from the lack of a distinctive therapeutics, but now possesses a surgical treatment firmly grounded in the essential intellectual discipline of neurology. No longer does the student need to look upon neurology as a sort of indoor diagnostic sport. Many of the major triumphs of neurosurgical surgery have been attained in the treatment of intracranial tumors, and the student should know just what can be accomplished in this field.

Two illustrations have been replaced by others which should be acknowledged — Fig. 126, Kennard (*J. Neurophysiol.*, 1944:7, Fig 6) and Fig. 147, Bramwell (*Intracranial Tumors*, Pentland, Edinburgh, 1888, Fig. 76). I am indebted to Mr. G. S. Adams for Figures 1, 26 and 30. It is a pleasure also to acknowledge the expert services of my secretary, Miss Beatrice Kahn, and of my photographer, Mr. Willard Huntzinger. Mr. Charles C Thomas has ever been ready to fulfil my slightest wish.

912 S. Wood Street,
Chicago, Illinois

PREFACE TO THE FIRST EDITION

The time is past when discussions of intracranial tumors as a whole can longer be profitable. It is true that such tumors, if allowed to develop long enough, have this in common that they give rise to intracranial hypertension. So may abdominal tumors cause enlargement of the belly, yet who would think of discussing fibroma of the uterus, carcinoma of the liver, and ovarian cyst as though they were similar lesions. The tumors which develop within the cranial cavity are also many and varied, and each must be studied and understood separately.

In this way we will gradually forget that we were taught to recognize as the cardinal symptoms of intracranial tumor, headache, vomiting, and failing vision. These are the symptoms of intracranial hypertension from whatever cause and the presence of tumor should, and can with increasing frequency, be diagnosed before these symptoms develop. There is only one cardinal symptom of tumor of the nervous system—a non-febrile, steadily increasing alteration in nervous function. There are exceptions—tumors may be accompanied by fever in the absence of infection, and with others the onset of symptoms may be sudden—yet one may readily learn when to suspect these exceptions and the general rule holds good. Whenever there is a steadily increasing focal alteration in nervous function the presence of a tumor should be suspected, and confirmed or excluded, long before the symptoms of intracranial hypertension appear, because the earlier the diagnosis is made the better are the chances of successful removal of the growth.

One should always in suspected cases make a three-fold diagnosis—the presence of tumor, its location, and its nature. The diagnosis of intracranial tumors is peculiarly difficult because of their enclosure within a rigid bony case, out of reach of the palpating finger. For a long time physicians were content to *differentiate tumor from gumma or tubercle*, but with the development of cerebral physiology they began also to make localizing diagnoses. Soon a tumor was correctly localized by Bennett from the symptoms alone and removed by Godlee (1884). Tumors were thereafter localized and removed with increasing frequency but the localization remained hazardous in many cases because of our still imperfect knowledge of cerebral physiology, and be-

cause of the tendency of the tumors to give rise to symptoms from distant parts of the brain by pressure and circulatory derangements. Even today no more than 80 to 85 percent can be correctly localized from the clinical symptoms alone. The localization of the remaining 15 to 20 percent has been greatly aided by Dandy, through the introduction of ventriculography and ceecephalography, so that lately the diagnosis of the nature of the growth has preoccupied the neurologist's attention. This pathological diagnosis can be made only by a knowledge of the biological peculiarities of each type of tumor.

A pre-operative knowledge of the pathological nature of the tumor to be operated on is of primary importance to the surgeon because each type presents different difficulties for removal. Surgeons have long since learned that they cannot remove certain tumors from the abdomen, but some of them are still attempting to remove perfectly unremovable tumors of the brain. And the operability of an intracranial tumor cannot be determined with certainty from its gross appearance. Familiarity with the various histological types is needed. Such knowledge is also necessary to establish a postoperative prognosis, yet a discussion of intracranial tumors from the pathological standpoint is to be found only in monographs, such as Cushing's "Tumors of the Nervus Acusticus," or in articles scattered in medical journals. In this small book I have attempted to present the subject of intracranial tumors primarily from the pathological standpoint. Much remains to be learned but a statement of our present knowledge it is hoped will be useful.

I have attempted to make only a simple and straightforward exposition for the use of the student of neurology. I claim no originality for this book except in the arrangement of the material. Therefore, I have dispensed with the constant citation of authorities which so encumbers the average medical book. The bibliography is intended as supplementary reading if the student desires to amplify his knowledge of any particular point; for this reason I have given references whenever possible to articles in English. I am not unfamiliar with, nor unappreciative of, the important works of continental authors but the North American student rarely reads anything but English with ease so that it is a waste of time to give him references in any other language. These lectures are an amplification of demonstrations and clinics which I have given to my students at the University of Chicago and the illustrative cases are from my own clinic, with few exceptions. The inclusion of some apparently extraneous material is due to the fact that in the University the subject

of intracranial tumors is taught as a part of a general course in oeuology and they demonstrate certain syndromes more clearly than other common neurological disorders.

I have paid small attention to operative technique. It is a subject of minor interest to the student and concerns only the specialist. It is, moreover, grossly over-emphasized in most manuals of surgery. There are many methods of opening the skull — for better or for worse. The really important matter is to know what to do once inside. What would one think of a surgeon who opened the abdomen without knowing the structure of its contents? Yet for some strange reason a surgeon will not hesitate to open the skull without an adequate knowledge of the structure of the brain, to say nothing of its functions and pathology.

The method of illustrating this book may cause some comment. It is printed on dull paper because I am tired of being blinded by the usual glossy paper used for medical books and I believe most medical students are equally annoyed by it. The use of dull paper made it impossible to illustrate with the usual half-tones. Pen-and-ink drawings have been found quite adequate except for the reproduction of roentgenograms. I know of only one way adequately to demonstrate roentgenograms and that is to bind the actual photographs into the book and supply a stereoscope for their examination. Roentgenograms of the head are usually useless anyway unless stereoscopic. Since this book aims only to instruct and not to support a scientific thesis, I have not hesitated to use diagrams and semischematic reproductions of roentgenograms.

With a vivid memory of the ponderous tomes which I bought as a student, and which still adorn my shelves with the pages uncut, I have tried, however short I may have fallen of my goal, to make a book which students will actually read.

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Chicago, Illinois

ACKNOWLEDGMENTS

The cases used as illustrative material in this book were referred to me by the following physicians to whom I wish to express my sincere gratitude.

Case I	Dr. Lemy Sloan	Case XXXVI	Dr. O. H. Horrall
II	Loren Avery	XXXVII	C. van Epps
III	George W. Hall	XXXVIII	Peter Bassoe
IV	O. Thürliman	XXXIX	E. P. Russell
V	W. van de Erve	XL	Joseph Brennemann
VI	Peter Kronfeld	XLI	Chas. Read
VII	Harvey Cushing	XLII	O. C. Ericksen
VIII	G. M. Peterman	XLIII	Paul Cannon
IX	Geo. W. Hall	XLIV	John Garvey
X	Peter Bassoe	XLV	Peter Bassoe
XI	Béla Halpert	XLVI	Geo. B. Hassin
XII	John Garvey	XLVII	Roy R. Grinker
XIII	Sidney Portis	XLVIII	J. G. O'Neill
XIV	C. van Epps	XLIX	Roy R. Grinker
XV	André Stapler	L	Stephan Poljak
XVI	Peter Bassoe	LI	Geo. C. Ellis
XVII	Geo. W. Hall	LII	John Garvey
XVIII	Henry Christensen	LIII	A. Rosenberger
XIX	Roy R. Grinker	LIV	Roy R. Grinker
XX	John Garvey	LV	W. H. Lipman
XXI	Richard Jaffé	LVI	E. V. L. Brown
XXII	Joseph Brennemann	LVII	Leroy Sloan
XXIII	M. G. Peterman	LVIII	W. H. Lipman
XXIV	H. W. Elghammer	LIX	Loren Avery
XXV	A. R. E. Wyant	LX	John Favill
XXVI	John Garvey	LXI	Peter Bassoe
XXVII	C. van Epps	LXII	Russell Wilder
XXVIII	Henry Christensen	LXIII	E. V. L. Brown
XXIX	Peter Bassoe	LXIV	Hans Reese
XXX	S. S. Stack, Jr.	LXV	A. Rosenberger
XXXI	Peter Bassoe	LXVI	Francis L. Foran
XXXII	Chas. H. Piper	LXVII	E. V. L. Brown
XXXIII	Peter Bassoe	LXVIII	Geo. W. Hall
XXXIV	Geo. W. Hall	LXIX	Geo. W. Hall
XXXV	Roy R. Grinker		

Most of the illustrations are original. The others have usually been modified, often extensively, from the following sources. Those copied more directly are also acknowledged in the subtitles. The upper illus-

tration in the frontispiece is from a drawing of E. Daleine after Andrea a Cruce, a surgeon who flourished in Venice about 1560. It is to be found as Fig. 34 in Vol. 1 of Chipault's *Chirurgie opératoire du système nerveux* (Rueff et Cie, Paris, 1894). The lower illustration of the frontispiece is from an operation at the Albert Merritt Billings Hospital in the year 1932. Fig. 1 is based on Cushing (*Am. Jour. Dis. Children*, 1927:33, Fig. 1); Fig. 4, Cushing (*Acta path. et microbiol. Scand.*, 1930:7, Fig. 4); Fig. 5, Cushing (*Am. Jour. Dis. Children*, 1927:33, Fig. 2); Fig. 6, Breschet (*Recherches sur le Système veineux*, Paris, 1830); Fig. 9, Key and Retzius (*Studien in der Anatomie des Nervensystems*, Norstedt, 1875, Bd. I, Tafel VII); Fig. 10, Locke and Naffziger (*Arch. Neurol. and Psych.*, 1924:12, Fig. 3); Fig. 13, Ingvar (*Brain*, 1923:46, Fig. 1); Fig. 22, Retzius (*Biologische Untersuchungen*, N. F. IX, Fischer, 1900, Tafel XII); Fig. 23, Spitzka (*N.Y. Med. Journal*, Feb. 2, 1901); Fig. 25, Cushing (*Johns Hopk. Med. Bull.*, 1901, Chart 3); Fig. 26, Foerster (*Zts. f. d. ges. Neurol. and Psych.*, 1930:125, Fig. 64); Fig. 27, Foix and Levy (*Revue neurol.*, 1927:2, Fig. 23); Fig. 29, Marie and Foix (*Revue neurol.*, 1917:1, Fig. 3); Fig. 42-a, McLean (*Zts. f. d. ges. Neurol. and Psych.*, 1930:126, Fig. 1); Fig. 42-b, Bailey (*Cowdry's Special Cytology*, 2nd Ed.: Hoeber, 2, Sect. XX, Fig. 2); Fig. 48-b, Cushing (*Pituitary Body and Hypothalamus*, Thomas, 1932, Fig. 19); Fig. 51, Cushing (*Idem*, Fig. 16); Fig. 54, Leblanc (*Travaux du lab. d'anat. de l'Univ. d'Alger*, 1926); Fig. 60, Key and Retzius (*Studien in der Anatomie des Nervensystems*, Bd. I, Norstedt, 1875, Tafel XXIX); Fig. 65, Schopper (*Frank. Zts. f. Path.*, 1913:13, Fig. 1); Fig. 66, Oayagi and Kyuno (*Neurologia*, 1912:11, Fig. 1); Fig. 67, Cushing (*Brain*, 1922:45, Figs. 13, 14, 15, 16); Fig. 78, Bassoe and Apfelbach (*Arch. Neurol. and Psych.*, 1925:14, Fig. 1); Fig. 80-a, Gamper (*Klin. Monatsbl. f. Augenh.*, 1918:61, Fig. 1); Fig. 80-b, Scarlett (*Arch. Ophth.*, 1925:54, text plate 6); Fig. 86, Cushing and Bailey (*Blood vessel tumors of the brain*, Thomas, 1928, Figs. 60, 61, 62); Fig. 87, Hortega (*Boletín de la Soc. esp. de Biología*, Nov. 1919); Fig. 98-b, Herrick (*Arch. Neurol. and Psych.*, 1924:11, Fig. 10); Fig. 103, Cushing (*Surg. Gyn. Obst.*, 1931:52, Fig. 15); Fig. 111, Herrick (*Introduction to Neurology*, Saunders, 1915, Fig. 77); Fig. 123-b, Horrax and Bailey (*Arch. Neurol. and Psych.*, 1928:19, Fig. 9); Fig. 125, Cushing (*Pituitary Body and Hypothalamus*, Thomas, 1932, Fig. 17); Fig. 126, Ranson (*Anatomy of the Nervous System*, Saunders, 1925, Fig. 196); Fig. 127, Dejerine (*Sémiologie des affections du système ner-*

veux, Masson, 1914, Figs. 50, 55); Fig. 128, Buckley (*Arch. Path. and Lab. Med.*, 1930:9, Fig. 10); Fig. 130, Pollock and Davis (*Jour. Comp. Neurol.*, 1930:50, Fig. 3); Fig. 132, Draganesco (*L'encéphale*, 1929:24, Figs. 1, 2, 3); Fig. 136, Davis (*Jour. med. Research*, 1924:44, Fig. 10); Fig. 137, Kinnier Wilson (*Brain*, 1906:29, Fig. 5); Fig. 148, van Wagenen (*Arch. Neurol. and Psych.*, 1927:17, Fig. 18); Fig. 149, Kaufmann (*Pathology*, Blakiston, 1929:3, Fig. 953); Fig. 151, Homans (*Textbook of Surgery*, Thomas, 1931, Fig. 262); Fig. 152, Parker (Mayo Clinic), (*Arch. Neurol. and Psych.*, 1927:16, Fig. 1).

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My indebtedness to numerous students of neoplastic growth in the brain is obvious. I should mention in particular, however, my debt to my former master, Harvey Cushing. Most that I know about intracranial tumors I learned while in his clinic or in charge of his laboratory. My associates, Drs. R. R. Grinker, Stephen Poljak, P. C. Bucy, and Douglas Buchanan have all read parts of the manuscript. I have profited greatly by their suggestions. I should mention also my friends Drs. Peter Kronfeld, Chas. Swift, C. J. Herrick, H. G. Wells, John Fulton, Cobb Pilcher and Sidney W. Gross. However, they should be held responsible for the merits only of the book, not for its defects, since I have not always followed their advice.

My secretary, Miss Josephine Newson, has been indefatigable in the preparation of the manuscript. The index is the work of Dr. Sidney W. Gross. The illustrations were mostly drawn by Miss Gladys McHugh. The microscopical work has been done by Miss Catherine Mahoney. The graphs were kindly prepared for me by Mrs. Julia Scammon. Last but not least I must mention my genial publisher, Mr. Charles C. Thomas, whose devotion to the production of books which should be both beautiful and useful is well known.

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INTRACRANIAL TUMORS

CHAPTER 1

THE PROBLEM OF TUMORS IN GENERAL

ITS RELATION TO INTRACRANIAL TUMORS

The word tumor, in its general sense, means only a swelling, whether produced by fluid, heaping up of tissues, collection of chemical substances or otherwise, but we use it in the sense of an autonomous new growth of tissue—a neoplasm. In beginning our study of intracranial tumors we need to place them in their proper perspective with regard to the problem of tumors in general. This is all the more necessary because in most general discussions of tumors those of the brain are disregarded. In a recent survey of the question of cancer (187) they were not even mentioned, yet the problem of neoplastic growth is the same in the brain as elsewhere.

The brain is a common site of origin for neoplasms. In an analysis (510) of 15,481 consecutive tumors from the records of Middlesex, University, St. Bartholomew and St. Thomas's Hospitals in London, 287 tumors of the brain were found, making about 1.8 percent. Of these 157 were in males and 130 in females. Whatever one may think of the value of such statistics (508) the figures show at least that tumors of the brain are more common than generally supposed.

Neoplasms develop within the body but somehow are not of it. They use the sources of nourishment of the body yet are, nevertheless, alien to it and may even destroy it. The first insight into how this might occur was incorporated into the THEORY OF EMBRYONIC RESTS, according to which tumors arise from groups of cells which have become isolated and arrested during embryonic life and later pursue an independent development. This theory was consistent with the fact that the cells of many tumors manifest a fertility usually found only in embryonic cells, and with the observation long before made that rudimentary undeveloped structures which have not completed their differentiation, in fact all the unusual accidental tissues of the body, are frequently the site of tumorous growth. With the passage of years evidence has constantly accumulated in support of this hypothesis, at

least for some tumors. Groups of such isolated and arrested cells, called rests, are frequently found in all parts of the body where tumors are apt to develop. Several hundred such abnormalities might be listed (187) such as misplacement of a portion of one organ into another, supernumerary organs, remnants of embryonal organs, superfluous cells at mucocutaneous junctions and misplaced germinal cells.

In the intracranial cavity also a relationship between embryonal tissues and tumors may readily be demonstrated. The epithelial portion of the hypophysis develops from an out-pocketing of the buccal cavity but its cells undergo a transformation entirely different from that of the buccal epithelium, with the exception of isolated nests of epithelial cells around the stalk. And it is just here in the neighborhood of the hypophysial stalk that there occurs an epithelial tumor which so resembles in structure the adamantinoma of the buccal cavity that it is often called by the same name. The relationship of these tumors to the epithelial rests of the hypophysial stalk was long ago suggested (350). Also just behind the dorsum sellae is occasionally found at necropsy a slimy mass which communicates through a small opening with the interior of the clivus. It is called the ecchondrosis physalifera, and has been proved to be a surviving remnant of the notochord. In exactly this situation a tumor develops whose structure resembles that of the notochord and so is called a chordoma (39). Another intracranial tumor whose structure is adequately explained by the theory of embryonic rests is the pearly tumor (31). A mass of epithelial cells without blood-supply, it seems a perfect example of what might be expected to happen if a group of squamous epithelial cells became isolated in the subarachnoid space and continued to multiply. More complicated epidermoids and dermoids are also rarely found in the intracranial cavity and even teratomas (282) occur there.

It is evident that the younger the cells of the embryonic rest are, the more complicated may be the structure of the tumor arising from them. The cells which give rise to a teratoma, for example, must be less differentiated than those which form an epidermoid. In the same way a tumor of the brain which contains both neurones and neuroglial cells must have arisen from more embryonic cells than those which are the origin of tumors composed solely of neuroglia (46).

Experiments on animals have added further evidence in favor of the theory of embryonic rests. Fragments of embryos transplanted into animals of the same species continue to grow for a certain time and

form tumors, mainly cystic, resembling in structure the cystic tumors of the ovaries and testes (215). But these experiments, while supporting the theory, also emphasize its weaknesses. The tumors, usually cystic, resulting from transplantation of embryonic tissue grow for only a short time and then remain as local indolent masses or even regress. It is known also that teratomas are in general benign local growths even within the intracranial cavity. The theory obviously does not explain why some tumors are of a benign nature, causing trouble only by their size, while others are more malignant, invading and destroying the normal tissues.

Moreover, for many tumors no rests are to be found. To remedy this latter inadequacy of the theory it has been supposed that any cell within the body which remains in a relatively undifferentiated state, whether misplaced or not, is more liable to become neoplastic. Many illustrations might be given in support of this hypothesis, such as the frequency with which tumors arise from the basal cells of the epidermis, or the endometrium of the uterus. A possible example in the intracranial cavity is furnished by the frequency with which adenomas arise from the undifferentiated or "reserve" cells of the hypophysis (171). Similar undifferentiated cells in the brain were supposed to give rise to gliomas. They were called by such names as rounded cells or cuboid cells, but it is now known that their embryonic appearance was due to the lack of satisfactory technique for demonstrating their cytoplasm.

Much stress was placed also on the idea of mechanical separation of cells, making the isolation of cellular groups a process which might occur in adult life from traumatism or otherwise. But even these supplementary hypotheses do not explain why certain cells, either in rests or in their normal places in the body, suddenly take on the property of unlimited growth to form a malignant tumor — a *cancer*. Many theories have been advanced to account for this sudden assumption of neoplastic growth. They may be divided into those which place emphasis on an external factor and those which stress an internal factor within the cell.

The proliferation of cancerous cells seems to be unlimited. A cancer of mice by repeated transplantation has been kept growing for more than thirty years. This fertility of the cancerous cells has caused them to be likened to embryonic cells and has given rise to the THEORY OF CELLULAR AUTONOMY. But there is this important difference, that the fertility of embryonic cells diminishes and disappears as differentiation

occurs, and the adult organism is completed, while the cancerous cells continue to multiply often without differentiation. Nevertheless many cells of an adult organism still have the ability to proliferate under certain circumstances. Lower animals are able to reconstruct entire parts of the body which have been destroyed or removed. Many simple tissues of the human body have proliferative capacity of no mean order although the human being cannot reconstruct complicated organs. The powers of growth autonomous in these cells seem to be held in check by various restraining influences whereas the cancerous cells act as though their restraints were absent or powerless.

Those influences which restrain the growth of cells have been investigated. One of the most important is the organization of cells into complex tissues. It has been shown in many ways that the relationships of cells to others in multicellular organisms are very important for growth. The cells of neoplasms seem to have lost this control by the organism as a whole. One way in which the organism makes its influence felt is undoubtedly in the distribution of nourishment. Chemical researches have led to the hypothesis that the neoplastic transformation of a tissue results when its cells acquire the ability to grow anaerobically with a fermentative type of metabolism (498). The development of a specialized function by any cell also limits its possibilities of growth; it seems that the energy available for growth is used up by the special function. An example of this restraint may be found in the case of the pituitary adenoma. It is known that the chromophile adenoma grows more slowly and usually reaches a much smaller size than the chromophobe adenoma. There are many reasons to believe that the chromophile tumor is composed of actively secreting cells (171). Sometimes the restraint seems to be a purely mechanical one. For example, the skin, constantly proliferating, is held in check by the dense corium and grows only outwardly, but if the resistance of the connective tissue is weakened by the injection of a lipoid solvent the epithelium grows also inward (89). Tumors often seem to grow more rapidly after a dense capsule has been incised. It is a fact often remarked by surgeons that brain-tumors seem to grow much more rapidly after a decompressive operation has been performed and the intracranial tension released.

But it would seem that the proliferative possibilities of many neoplastic cells far exceed any power autonomous in the cells themselves. To account for the excess some have supposed that the neoplastic cells

have been fertilized. The hypothesis is based on the well established facts of the rejuvenation of the sexual cells after fertilization and of certain unicellular organisms after conjugation. This reawakening of reproductive function in a somatic cell has been thought to be brought about by fertilization by leucocytes or by nuclear conjugation. These fanciful conceptions have not been generally accepted. Recently studies in the artificial culture of tissues have led to the demonstration of chemical substances which stimulate growth. It is but natural that such substances should be sought for in cancers (90).

Many simpler ways are known to heighten the proliferative activity of cells. One of the most definitely established is CHRONIC IRRITATION. It has long been maintained that certain types of tumor result from continued irritations; such are the cancers of chimney-sweeps, paraffin-workers, cotton-spinners and x-ray technicians (80). Experimental support for the theory of chronic irritation is supplied by the results of long-continued application of coal-tar to the rabbit's ear which finally provoked a malignant epithelioma (517). Cancer of the stomach had previously been produced in rats by feeding them cockroaches infested by *Spiroptera neoplastica*. A chronic irritation resulted, followed by papillomatous formation and then occasionally by a malignant invasive neoplasm. There are many other examples of neoplastic processes caused in animals by parasites. Recently mammary cancer has been produced in the mouse in a manner more nearly resembling the supposed mechanism in man by causing stagnation of the milk in the actively breeding animal (15). While a chronic irritation results primarily in a simple hyperplasia of the tissue, there is now abundant evidence that on the basis of such a hyperplasia a malignant neoplasm may arise.

Recently numerous carcinogenic substances have been isolated, by means of which neoplasms are readily provoked. Even gliomatous tumors have been produced in this way (429). It is difficult to imagine what might be the chronic irritation which would so affect the intracranial contents in man. In this case it is generally admitted that a single trauma may be a sufficient irritant to start a neoplasm. Yet when the evidence is examined carefully it is not at all convincing (369). Certainly the percentage of intracranial tumors was no higher among the veterans of the World War than in the general population and yet the number of cranial injuries was much higher. In the case of one hundred and fifteen tumors observed in a hospital in Hamburg (496) no traumatic accident

worthy of mention could be found in one hundred and one cases, in seven others the tumor existed certainly before the trauma, and in the seven remaining the relation between the accident and the beginning of the tumor was far from clear. It is much more probable that the *trauma serves merely to call attention to a preëxisting tumor by aggravating its symptoms.*

There is the possibility, however, that the irritating factor may be a microorganism of low virulence. The etiology of several peculiar diseases of lower animals, such as sarcoma of chickens, and myxomatosis of rabbits, may have some relation to specific microorganisms but one may question their true neoplastic nature. Certainly extensive search has not as yet revealed any organism characteristic of neoplasms in general. Yet the parasitic theory dies hard; late theories try to incriminate a filterable virus (238).

Even though a chronic irritant, such as a parasite or virus, were found to be always at work to initiate neoplastic transformation in an undifferentiated or misplaced cell the intimate mechanism of such transformation would still remain to be explained. This problem is one of cellular pathology and is being attacked actively by experimental cytologists. The mechanisms of cellular division and reproduction have been analyzed more closely and many theories have resulted, of which I may mention one which supposes that a cancer results from a trouble of the normal rhythm of cellular reproduction, particularly of the rhythm of mitosis. It postulates the existence of a regulating system within the nucleus which is transmitted in equal parts to the daughter-cells at the moment of division, not bipolar but tripolar or retrapolar, some of the daughter-cells receiving the regulatory system while others are deprived of it; the latter become cancerous.

THIS THEORY OF ABNORMAL MITOSIS, which makes of cancer a pure hazard, is contrary to the opinions of the believers in the hereditary nature of cancer. These partisans base their views on the supposed demonstration of families in which cancer is particularly frequent. Such studies of cancerous families have never been very convincing. So far, hereditary taint has been fairly clear only for a few tumors, such as generalized neurofibromatosis, multiple enchondromata, and glioma of the retina. No glioma of the brain has even been supposed to be hereditary, although there have been reported identical gliomas in the cerebellum of identical twins (311).

THE HEREDITARY THEORY has been strengthened by the results of

the study of cancer in animals. It is becoming increasingly evident that different species of animals have different tumors (507), for example, carcinoma of the mammary gland is very frequent in mice but rare even in the biologically closely allied rat and unknown in the cow whose mammary gland is constantly traumatized. And different species vary greatly in the ease with which tumors may be produced in certain organs by similar irritation. Carcinomas are readily provoked in the skin of mice by repeated irritation with tar but it seems impossible to cause similar cancers in the skins of rats or guinea-pigs. It has, moreover, been possible to breed strains of mice which are peculiarly susceptible to neoplastic disease as shown by the unusually high incidence of spontaneous cancer (506).

There seems to be some evidence of an influence of race on the incidence of certain tumors, for example, the Japanese are said to have mammary carcinoma rather infrequently. But there is no good evidence of any racial variation in the incidence of intracranial tumors. The supposed immunity of negroes to brain-tumors probably results from failure to diagnose. It has been recently stated (158) that Jews are unusually susceptible to the development of hypophysial adenomas. The statistics, however, were compiled in a clinic which receives an unusually high percentage of Jews from New York City.

From the foregoing it seems evident that, in a predisposed person, normal, misplaced or hyperplastic cells may undergo neoplastic transformation when chronically irritated. But neoplastic growth often occurs when no chronic irritation is evident and the hereditary predisposition is often impossible to demonstrate, at least for man. The intimate mechanism of this malignant transformation still escapes us. The resulting neoplasms vary greatly in their behavior. Many of them evolve locally; these are called benign. Cytologically these often resemble closely hyperplasias, from which they are distinguished mainly by their precise limits. Others invade and infect the surrounding tissues, even spreading to distant parts of the body to form new foci of growth known as metastases; these are said to be malignant and are called cancers. The malignant tumors are usually composed of more undifferentiated cells than those of the benign growths. This lack of differentiation is generally interpreted to mean that such tumors have arisen from more embryonic cells. But it is also possible that the neoplastic cells in their growth have "dedifferentiated." The transformation of a benign tumor into a malignant cancer is frequent. In the intracranial cavity the "dedifferentiation"

of the cells of gliomas, as the tumors increase in rapidity of growth, has often been observed (468). As its malignancy increases the cells of a cancer are not only more undifferentiated but, due to the abnormal conditions under which they grow, various anomalies occur such as hyperchromatic nuclei, abnormal chromosomes, disorientation or asymmetry or pluri-potentiality of mitosis and alteration of the nucleus-plasma ratio.

The spread of a malignant tumor in the body is presumably the result of two factors: the capacity of its cells to multiply, and the resistance of the body to it. One of the primary results of the growth of a tumor is to excite the connective tissue to form a dense capsule around it. Yet if the tumor is capable of breaking through the capsule, the connective tissue may actually aid the spread of the tumor by forming a stroma which acts as a framework for the nutrient vessels. The nature of the resistance of the body to neoplastic growth has been further analyzed by studying the mechanism by which a resistant animal absorbs a tumor-graft (327). In an unsusceptible animal the graft fails to excite the formation of a stroma and hence remains without suitable channels of nutrition. Also an inflammatory reaction is aroused in the neighborhood of the graft. This reaction is absent in susceptible animals. It indicates that the lymphocyte plays an important rôle in the resistance to tumor.

Animals may be rendered immune to transplantable tumor, but the mechanism of the formation of this immunity is not clear. It is known that antibodies are formed toward the cells of normal tissues, but in the sera of animals rendered immune to the transplantable tumors no specific cytolysons, agglutinins, or precipitins have been demonstrated. No complement-deviation tests have been successful. There seems to be simply a local and general hypersensitiveness produced in immunized animals by regression of inoculated tumor-tissue. Attempts to convey actively acquired resistance to other animals have not been distinctly successful.

These may be some of the reasons why *intracranial tumors do not metastasize to other parts of the body*, although they may spread widely in the subarachnoid spaces and even rarely invade the subcutaneous tissues when portions of the skull and meninges have been removed. Attempts to transplant them into animals have been unsuccessful as might have been expected. Very little experimental work has been done with brain-tumors because they are excessively rare in other animals than man (444).

In addition to provoking the organism to defensive reactions a cancer affects it in many other ways. Most cancers are accompanied by a progressive deterioration in the quality and quantity of the blood. The progressive emaciation and cachexia of malignancy are well known. These general degenerative changes have been supposed to be due to toxic substances given off by the cancerous cells. Such toxic changes do not accompany primary intracranial tumors and are sometimes of use in distinguishing between primary and metastatic tumors of the brain. If a tumor arises in a glandular tissue the cells may furnish a secretion having an effect similar to that of the normal gland. A good example is furnished by the hypoglycemic convulsions accompanying adenomas of the islands of the pancreas (445). In the anterior lobe of the hypophysis arises an adenoma composed of eosinophilic cells which is accompanied by a clinical syndrome known as *acromegaly*. A similar condition may be provoked in the dog by parenteral injections of extracts from the anterior lobe of the hypophysis. There is evidence that the active principle of this extract comes from the eosinophilic cells. It is therefore probable that the eosinophilic adenoma actually secretes.

All of these studies have made it evident that the etiological factors are variously combined for nearly all neoplasms. *It is increasingly apparent that different tumors are quite distinct clinical and pathological entities and that observations made on one may not safely be applied to another* (187). The classification of tumors is, therefore, of primary importance because entities must be isolated for study. But our knowledge is too limited at present to permit a pathogenic classification such as is given of infectious diseases. A purely embryological classification is also impossible. We are ignorant of much of the embryological development and the absolute verity of the theory of the three germinal layers is no longer admitted by histologists. Metaplasia and "dedifferentiation" of tissue make it difficult to be sure of origins. There are many difficulties also in the way of classifying tumors according to the tissues from which they arise. Some may arise from embryonal rests. Such a classification would be too general anyway and of little use practically. Tumors arising from the *leptomeninx*, for example, are very varied in structure and behavior, and can be subdivided histologically into mesothelial, fibroblastic, hemangioblastic, melanoblastic, osteoblastic, lipomatous, and perhaps other types (43). It is useless to insist that the typical cell is the fibroblast, so that they should all be called fibroblastomas. Such a designation does not explain their structural dif-

ferences and clinical variability.

But when one looks long and earnestly at a series of tumors they begin to group themselves according to certain familial resemblances of structure and behavior. Such a classification is imperfect but necessary in the present state of our ignorance. If we classify intracranial tumors in this way we come to some such a result as follows:

- | | |
|----------------------------------|-----------------------------|
| I. Encephalic tumors | 5. Melanoblastoma |
| a. Gliomas | 6. Hemangioblastoma |
| 1. Glioblastoma multi- | 7. Sarcoma |
| forme | b. Sheath-tumors |
| 2. Spongioblastoma polare | 1. Neurinoma |
| 3. Ependymoma | III. Hypophysial tumors |
| 4. Neuroepithelioma | a. Adenoma |
| 5. Astroblastoma | 1. Eosinophile |
| 6. Astrocytoma | 2. Chromophobe |
| 7. Oligodendroglioma | b. Craniopharyngioma |
| b. Glioneuromas | IV. Dysembryomas |
| 1. Medulloblastoma | 1. Teratoid cysts |
| 2. Ganglioneuroma | 2. Pearly tumors |
| II. Tumors of the covering cells | 3. Chordomas |
| of the nervous system (lopho- | 4. Pinealomas |
| stegomas) | 5. Papillomas |
| a. Meningeal tumors | V. Vascular tumors |
| 1. Meningothelioma | 1. Hemangioblastoma |
| 2. Fibroblastoma | (Lindau's type) |
| 3. Osteoma | 2. Angioma racemosum |
| 4. Lipoma | 3. Capillary telangiectases |

The frequency of the different types may be appreciated from the following table taken from recent statistics (129), although the system of classification is somewhat different from ours:

Gliomas	862— 42.6 percent
Neuroepithelioma	2
Medulloblastoma	86
Pinealoma	14
Ependymoma	25
Glioblastoma multiforme	208
Spongioblastoma polare	32
Oligodendroglioma	27
Astroblastoma	35

Astrocytoma	255	
Ganglioneuroma	3	
Unclassified	175	
Pituitary adenomas		360— 17.8 percent
Chromophobe	264	
Chromophile	73	
Mixed	23	
Meningiomas		271— 13.4 percent
Neurinomas		176— 8.7 percent
Congenital tumors		113— 5.6 percent
Craniopharyngiomas	92	
Cholesteatomas and dermoids	15	
Chordomas and teratomas	6	
Metastatic and invasive tumors		85— 4.2 percent
Granulomatous tumors		45— 2.2 percent
Tuberculomas	33	
Syphilomas	12	
Bloodvessel tumors		41— 2.0 percent
Sarcomas (primary)		14— 0.7 percent
Papillomas (choroid plexus)		12— 0.6 percent
Miscellaneous and unclassified		44— 2.2 percent
Total	2,023	100.0 percent

In the foregoing list the percentage of pituitary tumors is probably too high because they tended to congregate in that particular clinic. The percentage of metastatic tumors is lower than it would be in a general medical clinic. Perhaps the percentage of the malignant types of glioma is also too low (69). The inclusion of two types of infectious granuloma should be noted.

In most discussions of intracranial tumors these fifteen to twenty different pathological entities are discussed as a whole, according to the situation of the tumors within the intracranial cavity. Statistics arranged on this plan would look something as follows (135):

Cerebral	508
Pituitary	286
Cerebellar	178
Cerebellopontine	114
Brainstem	12

Skull

10

Total

1,108

From this analysis we could learn only that intracranial tumors are found most frequently in the cerebrum, certainly a meager and not very useful result.

If these same cases are analyzed according to age and the result put in the form of a graph the distribution is as follows (Fig. 1).

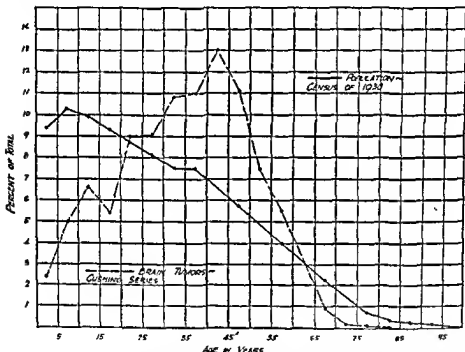


FIG. 1. Graph of age-distribution of intracranial tumors in relation to the population

This graph shows us that, since 9.8 percent of the population is between 10 and 15 years of age and develops 6.7 percent of all intracranial tumors whereas 6.5 percent of the population is between 40 and 45 years of age and develops 13.1 percent of all tumors, intracranial tumors are approximately three times as frequent at the older age-period per unit of population. This information that intracranial tumors predominate in middle life helps us very little in the diagnosis of any particular case because other diseases, often difficult to differentiate from tumor—for example, lues of the brain and vascular degenerations—predominate also in middle life.

These statistics indicate the futility of considering intracranial tumors as a whole. It is only when each pathological entity is studied separately that clear conceptions begin to emerge. To continue our analysis we will take the largest pathological group—the gliomas—and draw a graph for them according to the age of the patients.

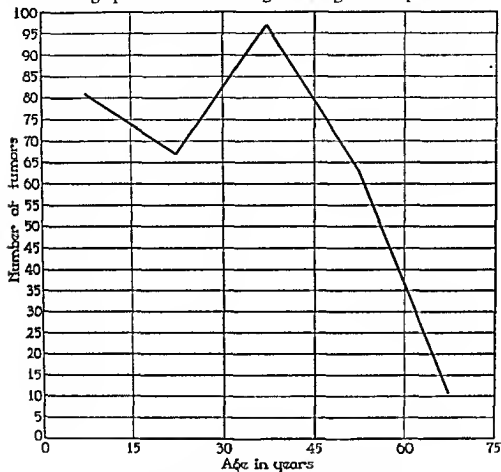


FIG. 2. Graph of age-distribution of gliomas.

There is a significant increase in the percentage of tumors in childhood and a sharp decrease in old age. These facts are useful in differential diagnosis, as we shall see later, but this graph is still not very illuminating because the group of gliomas is still too heterogeneous as will become very obvious when graphs are drawn for each pathological type of glioma. We shall take, for example, the medulloblastoma. A group of forty cases was distributed as shown in Figure 3, page 14.

We begin to appreciate the reason for the shift of the peak to the left in the previous graph. If we now analyze the medulloblastomas

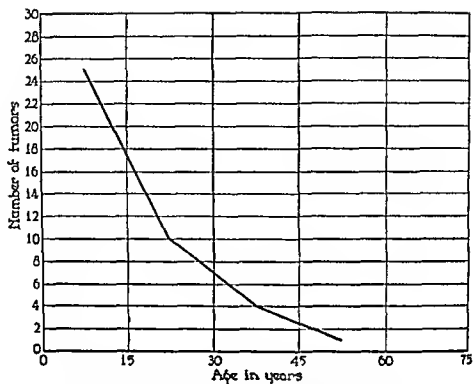


FIG. 3. Graph of age-distribution of medulloblastomas.

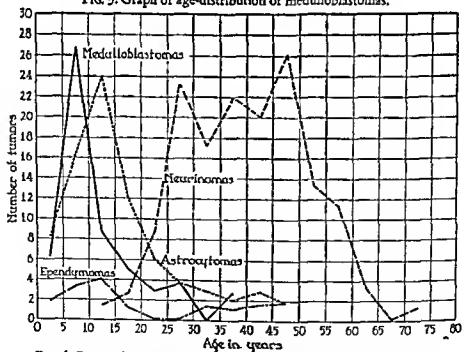


FIG. 4. Graph of age-distribution of most frequent types of subtentorial tumors (from Cushing).

according to location we get the following result: cerebrum 5, cerebellum 35. Whence it follows that the medulloblastoma is predominantly a tumor of the cerebellum of children, a truly significant finding.

If we try now to find out, for purposes of differential diagnosis, whether the other frequent types of subtentorial tumors predominate

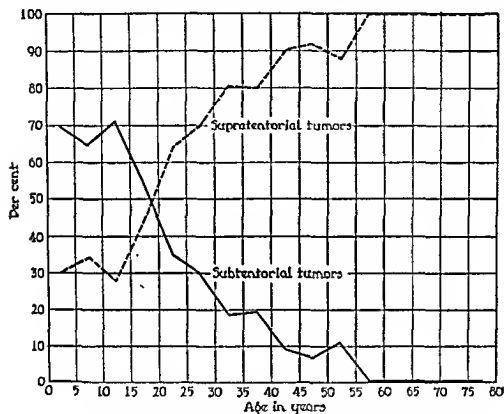


FIG. 5. Graph of age-distribution of gliomas according to location above or below the tentorium cerebelli (from Cushing).

in childhood we obtain a graph (Fig. 4), based on a much larger number of cases. It shows that the neurinoma is a tumor of adults, but that the subtentorial gliomas all predominate in childhood. This result is confirmed by an analysis of the whole group of gliomas which shows clearly that gliomas of the cerebellum are much more numerous in childhood (118) (Fig. 5). All studies of the intracranial tumors which occur during childhood arrive at the same result (41).

This difference in the site of origin of tumors at different ages is well known. An analysis (381) of 424 cases of tumor in early infancy showed that they were distributed as follows: eye and annexes

100, kidney 80, bones 67, brain 31, abdomen and pelvis 19, testes 15, liver 13, prostate 8, skin 8, intestine 7, neck 6, tongue 6, ovary 6, etc. In adults the most frequent sites are quite different (510): uterus 19.2 percent, mammae 17.5, skin 9.4, connective tissue 7.7, tongue and mouth 6.3, ovary 5.8, external genitalia 5.1, bones 4.0, rectum 3.3, stomach 2.6, lower lip 2.6, brain 1.8, etc. For malignant tumors (cancer) alone the figures are again different for adults (508) with carcinoma of the stomach leading the list.

Our study of intracranial tumors agrees, therefore, with the results of the study of other tumors. Neoplasms have one factor in common — autonomous growth — but they are otherwise widely different, and cannot profitably be treated as a group. *The group of intracranial tumors is also too heterogeneous to be treated as a whole. The origin, structure, symptoms, and treatment of each pathological entity must be studied separately.*

CHAPTER 2

STRUCTURE OF THE CRANIUM AND OF ITS CONTENTS

Before entering upon our study of the various types of intracranial neoplasms we must first review briefly a few fundamental anatomical and physiological conceptions. A thorough knowledge of the structure of the cranium and of its contents is essential for anyone who intends to deal with intracranial tumors and peculiarly so for the surgeon because the treatment of intracranial tumors is predominantly surgical. Yet this is not the place to furnish such detailed information; much must be supposed to be known to the student and is readily available in standard treatises on anatomy. I will take time to mention only a few peculiarities of structure which are of importance for the understanding of intracranial tumors and to describe in more detail some matters the descriptions of which seem to me difficult of access.

Much of the symptomatology of intracranial tumors results from their being enclosed within a practically rigid bony case, the calvaria, usually referred to loosely as the cranium, the vault of which is formed by the flattened parts of the occipital, parietal, temporal, and frontal bones. The floor of the intracranial cavity is in part formed also by the ethmoidal and sphenoidal bones. The bones of the vault come together along jagged irregular lines called sutures, and *union between them does not become firmly established until the tenth or eleventh year so that any increased intracranial tension before that age readily separates them*, with a resulting increase in the size of the head. Actual synostosis normally occurs only late in life.

In lower mammals the temporal and suboccipital muscles cover almost the entire calvaria but the increased size of the human brain has been so remarkable that these muscles are, in the human being, relatively greatly reduced in size and much of the calvaria is not covered by muscular tissue with the exception of the rudimentary platysma myoides. This last structure contains muscular fibers only at its frontal, occipital, and sometimes temporal extremities. For the most part it is reduced in man to a fibrous sheet known as the *galea aponeurotica*. The scalp, then, consists usually of the following layers from without inward: skin, subcutaneous fatty tissue, galea, loose areolar tissue,

periosteum. The galea is important to the surgeon because the blood-vessels of the scalp run within the fatty subcutaneous tissue, so that if the galea and skin are carefully approximated in closing a wound of the scalp there is no necessity to ligate the bloodvessels. The primary arteries of the scalp come from below and branch upward. This fact is made use of also in controlling hemorrhages in operations on the head and in planning incisions for intracranial operations, although the anastomoses between the arteries of the scalp are so numerous that it is not of essential importance. The nerves of the scalp also run from below upward and may be blocked readily, but again this fact is not of primary importance because anesthesia is usually obtained by local infiltration in the line of the incision.

The bones of the cranial vault have an inner and outer hard cortex separated by looser spongy bone called diploë, into which project the pneumatic extensions of the middle ear and nasal cavities. The mastoid cells and accessory sinuses must be avoided whenever possible in opening the cranial cavity because they are often infected. *The bones of the calvaria do not have single nutrient arteries as do the bones of the extremities.* Most of their arterial blood is supplied by small arterioles which arise from the deeper surfaces of the meningeal arteries in the depths of the meningeal grooves (291). A few other small arterioles penetrate the outer surface of the occipital and temporal bones, especially along the attachment of the temporal muscle and below the superior curved line.

Most of the circulation of the bones of the calvaria is of venous nature as is evident at any cranial operation. Innumerable small venous radicals in the diploë collect into larger channels known as the DIPLOIC VEINS. These channels are small in young individuals but become more evident in old age. They may be seen in any roentgenogram of the head. In general there is one such diploic vein for each bone; its distribution is shaped like a V with the point downward (Fig. 6). The caliber of the diploic veins varies markedly; their courses and distributions are very irregular. Usually they lie nearer the inner than the outer surface of the bone.

The *frontal diploic vein* drains the lateral half of the frontal bone and opens exteriorly into the veins of the scalp at the supraorbital notch. It may anastomose with its fellow of the opposite side. The *occipital diploic vein* similarly drains the lateral half of the occipital bone and opens externally into the muscular veins just below the

superior curved line. It anastomoses freely with its fellow of the opposite side and with the *parietal diploic vein*. The latter varies a great deal in its course and distribution. There seems often to be a *stellate radiation* from a central point in the parietal region and the largest draining channel sometimes runs backward into the occipital region and again downward behind the ear to the mastoid emissary or even

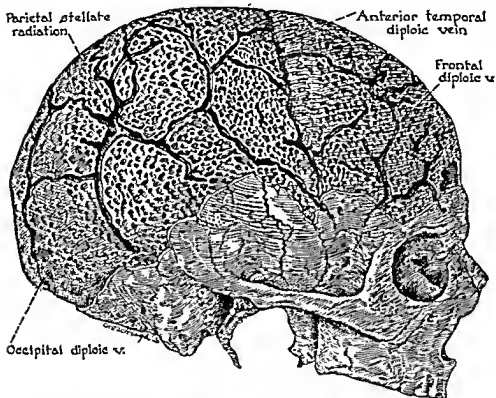


FIG. 6. The diploic veins. The outer table of the bones of the calvaria has been removed (after Breschet).

forward to the temporal vein. The *temporal diploic vein* has the same general direction as the anterior branches of the middle meningeal veins and anastomoses freely with them through the inner table of the temporal bone. Indeed they often form a single channel in the bone known as the sinus of Breschet. They also empty outward into the venous plexus of the pterygoid fossa. In addition to these outward terminal communications of the diploic veins into the external venous plexuses, there are numerous inward anastomoses with the venous channels in the dura mater, aside from those in the temporal region, especially along the superior sagittal sinus.

The inner periosteum of the cranial bones is at the same time the outer covering of the brain. The coverings of the brain are called meninges and of these there are two, the pachymeninx or dura mater on the outside and, within it but separated by a potential cavity known

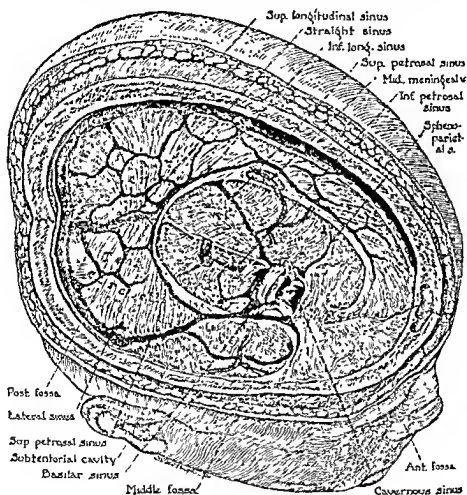


FIG. 7. The dural septa and intracranial cavities.

as the subdural space, the leptomeninx. The latter contains the clear cerebrospinal fluid which separates it roughly into two sheaths—an outer, the arachnoidal membrane, and an inner, the pia mater.

The pachymeninx is closely applied to the inner surface of the cranial vault for which it serves as a periosteum, but is readily sep-

parated in young adults except along the superior sagittal region. In the infant the pachymeninx is not yet separated from the scalp over the fontanels and cranial sutures and in old age it again becomes much more adherent to the inner surface of the calvaria. In addition the pachymeninx forms a series of rigid DURAL SEPTA which divide the

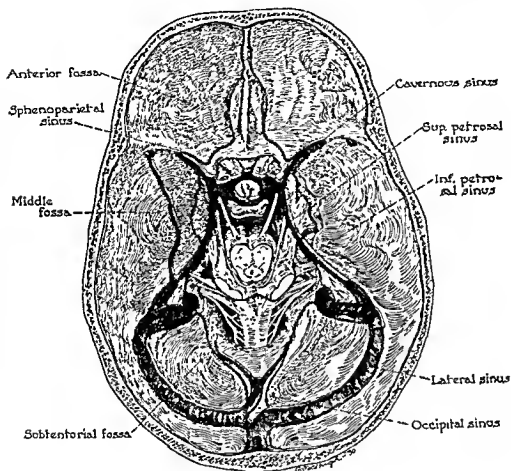


FIG. 8. The base of the intracranial cavity with the brainstem in place, midbrain retracted and dural attachment indicated.

intracranial cavity into subordinate cavities (Fig. 7). Of these the most important is the *tentorium cerebelli* which lies between the cerebellum and the occipital lobes of the cerebrum, dividing the intracranial cavity into the subtentorial and supratentorial cavities between which the incisura tentorii allows the passage of the brainstem. The tentorium stretches across from one petrous pyramid to the other and arches up-

ward, being held up by another rigid septum, the *falx cerebri*, which arches forward between the cerebral hemispheres. The latter is much more important posteriorly and becomes deficient at its anterior extremity. There is also a less important sheet of dura mater which covers the sella turtica, separating the brain from the hypophysis cerebri. It is called the *diaphragma sellae*. The rigidity of the dural septa should be appreciated. When the brain is displaced or distorted, the pressure of the edges of these septa may cause misleading symptoms (298).

The pachymeninx is irregularly adherent over the base (487) of the cranial cavity (Fig. 8) and hugs the uneven surface to form a series of depressions in which the various parts of the brain lie—the *frontal or anterior fossae* for the frontal lobes, the *middle or temporal fossae* for the temporal lobes, and the *posterior or occipital fossae* for the occipital lobes of the cerebrum. Beneath the tentorium lies the *cerebellar fossa* often spoken of loosely as the posterior fossa.

The *dura mater* is sensitive only around the basal region, the sensory nerves coming mainly from trigeminal branches and accompanying the meningeal arteries, which are themselves quite sensitive. The bloodsupply of the *dura mater* comes mainly from the *middle meningeal artery*. The anterior meningeal branch of the ophthalmic artery supplies a small area in the frontal region, and the mastoid branch of the occipital artery most of the subtentorial region. There are minor additions by branches of the internal carotid, lachrymal, ascending pharyngeal, accessory meningeal, and vertebral arteries. The course and branches of the middle meningeal artery are clearly illustrated in any textbook of anatomy, but insufficient emphasis is placed on the richness of its anastomoses. It even communicates freely across the superior longitudinal sinus with the meningeal artery of the opposite side. Contrary to a common opinion it does not supply blood to the arachnoidal granulations. *This artery may run some distance in actual tunnels within the temporal bone.*

The blood from the pachymeninx is collected by veins which accompany the meningeal arteries for the most part. The *middle meningeal veins* are particularly important. One often finds two large channels which communicate with each other and with the diploic veins. They follow in general the course of the anterior branch of the middle meningeal artery, arising from the lateral lacunae of the superior longitudinal sinus and leaving the skull by the foramen spinosum.

But aside from the meningeal veins proper there are in the *dura*

mater larger venous sinuses of much greater importance since through them drains most of the blood from the brain and much of the blood from the cranium as well. The DURAL SINUSES are cavities in the dura mater. They are not collapsible but are held rigidly open by the septa of the pachymeninx. The largest is the *superior longitudinal sinus* (Fig. 7) which begins by the confluence of small radicles near the crista galli and extends backward along the midsagittal line just under the vault of the skull at the upper border of the falx cerebri. This sinus is roughly triangular in outline and increases in size as it extends backwards. It receives the superior cerebral veins and communicates by a series of small openings with irregular cavities, in the dura mater on either side, which are known as LACUNAE (Fig. 16). These vary in size and number in different persons but are most prominent in the central region and may extend as much as 3 cm. lateral to the sagittal sinus (420). They drain laterally through the meningeal veins and medially into the sinus. The superior cerebral veins are closely adherent to their internal walls but do not empty into them. Their inner walls are very irregular because of the protrusion into them of innumerable arachnoidal granulations. The diploic veins communicate with them through their outer walls. The superior longitudinal sinus usually occupies a depression in the inner table of the calvaria and the lacunae also often cause considerable depressions which may be mistaken for pathological erosions. At the internal occipital protuberance the superior longitudinal sinus sometimes joins the straight sinus to form a large venous lake known as the confluens sinuum; more often it joins the right branch of the straight sinus, sending only a small channel to the left transverse sinus (181).

The *straight sinus* occupies the line of junction of the falx cerebri and the tentorium cerebelli. It branches usually at the internal occipital protuberance, the right branch joining the superior longitudinal sinus to form the right lateral sinus; the left branch continues as the left lateral sinus. At its origin the straight sinus receives a small and inconstant channel which runs along the inferior border of the falx cerebri—the *inferior longitudinal sinus*—and the great cerebral vein (of Galen). The *lateral sinuses* run along the posterior extremity of the tentorium cerebelli until they reach the petrous pyramids and then curve downward to pass out through the jugular foramina and become the internal jugular veins.

Over the base of the cranium are irregular venous channels in the

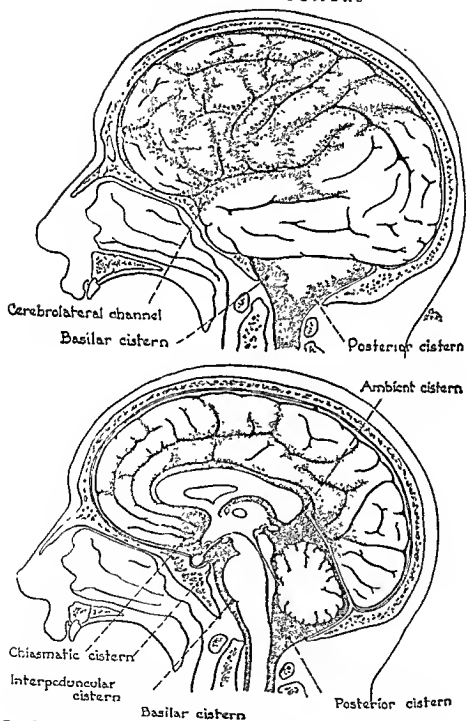


FIG. 9. Schematic representation of the principal collections of cerebrospinal fluid—above on the lateral surface, below on the median surface of the brain.

dura mater (Fig. 8). A small inconstant *sphenoparietal sinus* runs along the lesser wing of the sphenoidal bone to empty into an extensive venous cavity around the sella turcica—the *cavernous sinus*. The latter surrounds the carotid arteries and abducens nerves. In its lateral wall lie the oculomotor, trochlear, and ophthalmic nerves. It empties through irregular venous channels over the clivus into the *inferior petrosal sinus* which passes out through the jugular foramen to join the internal jugular vein. Another more constant channel, the *superior petrosal sinus*, passes backward and laterally along the upper border of the petrous pyramid to empty into the lateral sinus. There are sometimes small lacunae in the tentorium cerebelli which connect with the lateral sinuses.

There are also communicating channels called EMISSARY VEINS in the occipital region which connect the lateral sinuses, near the confluens, directly through the cranium with the muscular extracranial venous plexuses. Other emissary veins just back of the mastoid processes connect the lateral sinuses with the occipital veins and in the parietal region the parietal emissary connects the superior longitudinal sinus with the extracranial venous circulation. There are other such emissary veins in the base of the cranium, passing through the foramen ovale, spinosum, lacerum and canalis condyloideus. Finally it should be remembered that the vena ophthalmica superior, which drains most of the orbit and eyeball, passes inward through the fissura orbitalis superior into the cavernous sinus. These various venous anastomoses are very important for the study of the spread of infections and *in cases of intracranial tumor serve as accessory channels for venous drainage so that there is occasionally a tremendous dilatation of the veins of the scalp.*

The leptomeninges is hollow. The inner surface is attached to the outside of the brain and closely follows its irregularities. The outer surface is adjacent to the dura mater. Various delicate septa pass between the inner and outer layers but the intermediate (subarachnoid) space is mainly filled by the cerebrospinal fluid which everywhere intervenes between the pia mater and the arachnoid membrane. Since the contour of the brain is quite different from that of the dura mater, the subarachnoid space is in many places much wider than in others. These widened spaces are called *cisterns* (325). The most important cisterns lie along the base of the skull (Figs. 9 and 10).

As the SUBARACHNOID SPACE is followed upward from the cavity

of the spinal canal anterior to the cord it is seen to spread out beneath the brainstem. At the level of the pons it is broad and shallow in its middle portion but deepens in the cerebellopontine angles to form the *lateral cisterns*. Between the cerebral peduncles anterior to the pons it is deeper and is known as the *interpeduncular cistern*. Still further forward in the region of the optic chiasm it is even deeper to form the *chiasmatic cistern*. This whole space under the brainstem is

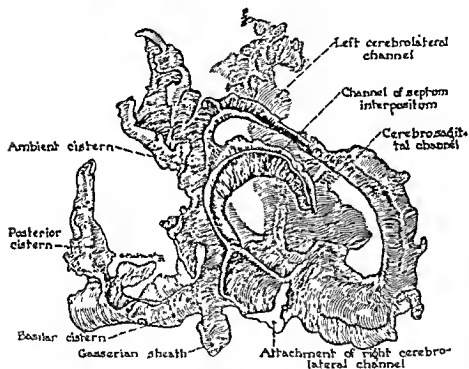


FIG. 10. Cast of the cisterns of cerebrospinal fluid (after Locke and Naffziger).

sometimes spoken of as the *basal cistern*. From the basal cistern the sub-arachnoid space may be followed upward and outward over the brain. The large channels are as follows: in the bulbar region a small channel passes upward over each cerebellar hemisphere. Also laterally the space extends as sheaths around the ninth, tenth, and eleventh nerves and around the seventh and eighth nerves. Farther forward a similar but larger sheath surrounds the fifth nerve and gasserian ganglion. From the chiasmatic cistern the large and important *cerebrolateral channels* curve outward, then upward and backward along the lateral fissures on either side. Also the anterior extremity of the chiasmatic cistern

continues upward between the frontal lobes, then curves backward over the callosal body to form the *cerebrosagittal channel*. It continues on around the splenium to enter an enlarged space called the *ambient cistern* in the region of the pineal body. From the ambient cistern a channel passes forward in the triangular space between the callosal body and the roof of the third ventricle, and two paired channels laterally

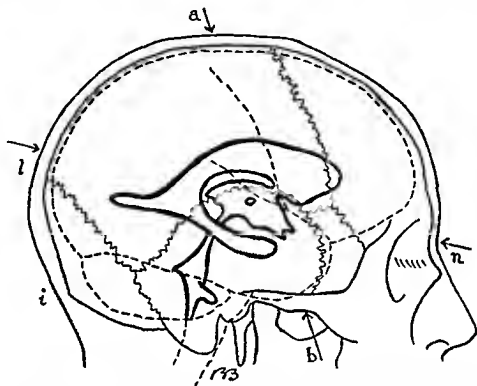


FIG. 11. Scheme of the relationships of important intracranial structures to the exterior of the skull. The ventricles are outlined by heavy black lines and the brain by interrupted lines. i, inion; l, lambda; n, nasion; a-b, line indicating the location of the central cerebral sulcus; l-n, line indicating the location of the lateral cerebral fissure.

around the midbrain, in the great cerebral fissures, downward and forward to connect with the basal cistern. A median channel also extends backward above the cerebellum to end in a large and important cerebellomedullary, or *posterior cistern*, which lies in the angle between the cerebellum and the dorsal surface of the bulb. From these main channels smaller passageways extend between the convolutions into the various sulci of the cerebral hemispheres, seeming to be smaller in the occipitoparietal region than elsewhere.

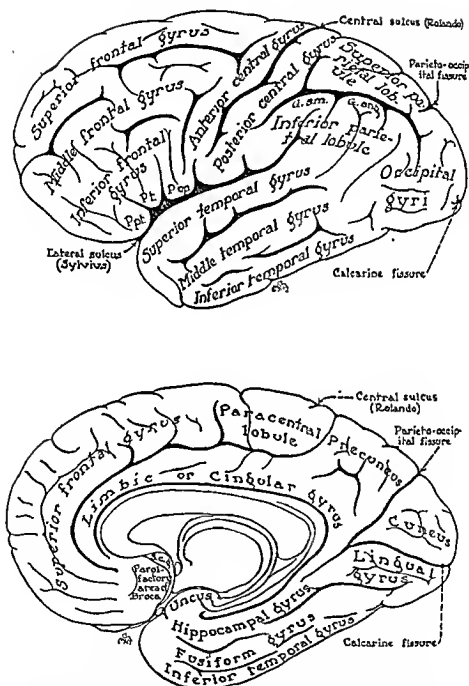


FIG. 12. Scheme of the gyri of the cerebral cortex—above, on the lateral surface; below, on the median surface. G. sm.—gyrus supramarginalis G. ang.—gyrus angularis.

The surface of the cerebrum is much corrugated with irregular worm-like CONVOLUTIONS separated by depressions called sulci or fissures. It is necessary that the surgeon be able to distinguish the convolutions, because injury to certain of them is very disastrous. In earlier times, when the surgeon dared to make only a small trephine opening, it was important to know as minutely as possible the relationship of the gyri to the external surface of the calvaria. At the present time, when large areas of the brain are exposed at operation, such minute cranio-cerebral topography is unnecessary and the elaborate schemes which filled pages in earlier treatises on cranial surgery are obsolete. It is enough to know in a general way the location of the lateral fissure and central sulcus to expose any given convolution (Fig. 11). The *lateral fissure* lies approximately under the line drawn on the surface of the calvaria from the angular process of the frontal bone to a point a centimeter or so above the lambda (junction of the occipital and parietal bones in the midline of the skull). The *central sulcus* may be located by drawing a line from the middle of the zygoma upward and backward to meet the sagittal plane of the calvaria 1 cm. behind the midpoint between the nasion and the inion. The central sulcus lies along this line above its juncture with the previously mentioned line locating the lateral fissure.

The names and relationships of the principal cerebral gyri and fissures, as we shall employ them, may be learned by reference to figure 12. A detailed description of them is unnecessary for our purposes and may be readily found elsewhere.

The adult human *cerebellum* is made up of numerous narrow lamellae, arranged in a seemingly haphazard manner, for which a fantastic terminology was long ago invented. It is impossible to apply these terms to the cerebellum in other vertebrates, but a common terminology applicable to all vertebrates has been worked out by comparative neurologists (287). Its relationship to the subdivisions of the human cerebellum is shown in Figure 13. The mammalian cerebellum may be thus divided into three fundamental lobes, of which the anterior and posterior are phylogenetically older. The *anterior lobe* includes the *lingula* and *vinculum lingulae*, the *lobulus centralis* and *alae lobuli centralis*, the *culmen monticuli* and *lobulus quadrangularis (pars anterior)*. The posterior lobe includes the *pyramis*, the *uvula*, and the *nodulus* with the *flocculi*. The identity of the *paraflocculus* is rather uncertain in man. The phylogenetically younger part of the cerebellum is in-

cluded in the middle lobe, which may be further subdivided into lobus simplex (lobulus quadrangularis—pars posterior—and declive monticuli), lobus mediodianus (folium and tuber), lobus ansoparamegianus (lobuli semilunares inferior and superior, and lobulus gracilis). The lobulus biverter and tonsil are perhaps peculiar to man.

The surface of the brain is covered by tortuous veins and arteries. It is important to know them and the areas which they supply because occlusion of certain of them must be carefully avoided in operating on

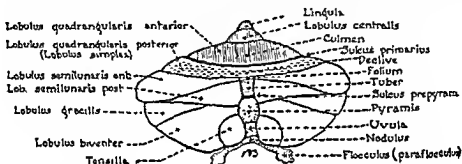


FIG. 13. Scheme of the cerebellum showing the principal subdivisions.

the brain lest serious neurological defects result. The ARTERIAL SUPPLY OF THE BRAIN is mainly by the internal carotid and vertebral arteries (65). The latter, after entering the intracranial cavity, unite to form the basilar artery which passes upward on the anterior surface of the brainstem. Just back of the dorsum sellae it bifurcates to form the posterior cerebral arteries. The internal carotid artery divides mainly into two arteries—the anterior and middle cerebral arteries. A branch goes backward to join the posterior cerebral to complete the circulus arteriosus (of Willis), and another enters the inferior extremity of the choroid plexus of the lateral ventricle.

The branches of the cerebral arteries vary considerably in their origins and courses. But however much their courses may vary, the peripheral distribution of each principal artery is remarkably constant.

A. *The anterior cerebral artery* (Fig. 14) passes across the anterior perforated space, above the optic nerve, to enter the interhemispheric fissure where it gives off a small anastomotic branch to the anterior cerebral artery of the opposite hemisphere. It then passes along the medial surface upward and forward to the knee of the callosal body. It now follows the epicallous sulcus and lies along the top of the callosal body as far as the posterior third where it moves up to the

callosomarginal sulcus and follows this to the convex surface of the brain and ends in branches to the paracentral lobule and precuneus.

From the lateral surface of the artery, at about the level of the anterior communication, there arises the recurrent artery (12) which runs back along the main trunk to join branches of the middle cerebral artery going to the corpus striatum.

The branches of the anterior cerebral artery on the mesial surface of the cerebral hemisphere are as follows (196):

1. The orbital artery arises where the main trunk turns upward on the medial surface and spreads out over the orbital surface of the frontal lobe.

2. The frontopolar artery arises about a centimeter below the knee of the callosal body and supplies the mesial surface of the frontal lobe above the subrostral sulcus as far forward as the pole.

3. The callosomarginal artery arises at the knee and passes upward and then backward in the callosomarginal sulcus. It gives off the anterior internal frontal branch about the middle of the superior frontal gyrus, the middle internal frontal branch at the posterior extremity of the superior frontal gyrus and itself terminates as the posterior internal frontal artery. These three frontal branches all pass upward to the convex surface of the hemisphere. They may come off separately from the main trunk of the anterior cerebral artery.

4. The pericallosal branch continues backward over the posterior part of the callosal body to anastomose with a branch of the posterior cerebral artery.

5. Numerous small branches from the concave surface of the artery supply the callosal body.

The territory of the anterior cerebral artery includes the whole of the mesial aspect of the frontal and parietal lobes, as far back as the parieto-occipital fissure, and the subjacent white matter, knee and anterior four-fifths of the callosal body, septum lucidum, anterior pillars of the fornix and part of the anterior commissure, part of the head of the caudate nucleus, the anterior part of the two outer segments of the lenticular nucleus, and the anterior half of the forelimb of the internal capsule.

B. The *middle cerebral artery* is the largest branch of the internal carotid artery (197). It bends outward across the anterior perforated space and enters the depth of the lateral fissure (of Sylvius), lying in close contact with the insula. It then curves outward again to gain the

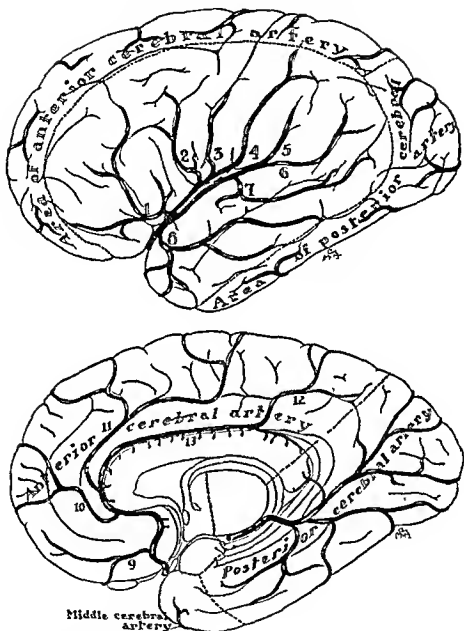


FIG. 14. Scheme of the arterial supply of the cerebral cortex— above, the lateral surface, below, the median surface. 1— orbitofrontal artery; 2— prerolandic artery; 3— rolandic artery; 4— anterior parietal artery; 5— posterior parietal artery; 6— angular artery; 7— posterior temporal artery; 8— anterior temporal artery; 9— orbital artery; 10— frontopolar artery; 11— callosomarginal artery; 12— posterior internal frontal artery; 13— pericallosal artery.

outer surface of the hemisphere. But it has by that time already given off its main collateral branches which come individually to the surface along the lateral fissure.

After some deep perforating branches to the basal ganglia it gives off superficial branches as follows (Fig. 14):

1. The anterior temporal artery arises a centimeter before the others, curves out of the lateral fissure and runs backward over the temporal lobe, giving branches to the anterior third of the temporal gyri. It helps also to supply the insula.

About a centimeter farther on usually arises a common trunk for the ascending arteries (although they may arise individually) as follows:

2. The orbitofrontal artery supplying the lateral part of the orbital surface of the frontal lobe and on the external surface the inferior frontal convolution except the superoposterior part of its posterior extremity.

3. The artery of the prerolandic sulcus runs for a few millimeters in the central sulcus (sometimes giving off a small arteriole to it) then curves over the anterior central gyrus to enter the pterolandic sulcus. It supplies the lower extremity and anterior lip of the anterior central convolution, the posterior extremity of the second frontal and superoposterior part of the posterior extremity of the third frontal gyrus.

4. The artery of the rolandic sulcus runs over the opercular part of the posterior central gyrus, then enters the central sulcus, irrigating the posterior border of the anterior central and the most anterior border of the posterior central convolution.

5. The anterior parietal artery curves over the opercular region, enters the intraparietal sulcus and continues in it, giving often a branch higher up which courses over to the central sulcus. It supplies the posterior border of the posterior central and the anterior portions of the other parietal convolutions, sometimes also the upper portion of the central sulcus.

All of these ascending arteries help to supply the insula. In addition the middle cerebral artery has the following branches:

6. The posterior parietal artery arises in the extremity of the lateral fissure and terminates in the gyrus supramarginalis and posterior part of the inferior parietal lobule. Its territory varies a great deal depending on the development of the anterior parietal artery.

7. The middle cerebral artery continues as the artery of the angular gyrus.

8. The posterior temporal artery descends in one of the short perpendicular branches of the lateral fissure and supplies the posterior two-thirds of the superior temporal and the posterior half of the middle temporal convolutions. Its territory is often much reduced by the anterior temporal artery.

It is important to note that the branches of the middle cerebral artery are arteries of sulci predominantly and irrigate the margins of the two adjacent convolutions. The territory of the middle cerebral artery includes also the upper part of the posterior limb and part of the anterior limb of the internal capsule, part of the head and the horizontal part of the caudate nucleus, and most of the lenticular nucleus.

C. The *posterior cerebral arteries* (Fig. 14) are the result of the bifurcation of the basilar artery. Each is directed outward and backward around the cerebral peduncle. After receiving the posterior communicating branch from the internal carotid artery it passes onto the inferior surface of the occipital lobe and divides into its terminal branches (198):

1. The anterior temporal branch is directed forward over the inferior surface of the temporal lobe where it supplies the anterior part of the fusiform gyrus and of the hippocampal convolution leaving free the tip of the lobe, which is supplied by the middle cerebral artery, and the uncus.

2. The posterior temporal branch is distributed to the rest of the inferior surface of the temporal lobe.

3. The voluminous posterior occipital artery runs buried in the calcarine fissure and supplies the postero-internal part of the occipital lobe, especially the lingual lobule and cuneus.

Before dividing into its terminal branches the posterior cerebral artery gives off a series of collaterals to the mesencephalon and basal ganglia. Their origins are diverse but each has a fixed terminal distribution. They are of great interest to physiologists since they supply practically all of the thalamic and peduncular regions, but concern us little in the symptomatology of brain-tumors. They supply half of the cerebral peduncle, the subthalamic region, the red nucleus, subthalamic body (of Luys), substantia nigra, the postero-inferior half of the thalamus, the superior cerebellar peduncle and the geniculate bodies.

The BLOODSUPPLY OF THE CEREBELLUM comes from three main pairs of arteries of which the first, the posterior inferior cerebellar artery,

arises on either side from the vertebral arteries just before the latter join to form the basilar artery (Fig. 15). The anterior inferior and superior anterior cerebellar arteries arise from the basilar artery. The branches of these cerebellar arteries anastomose freely with one another and the development of their various branches varies so considerably that no characteristic symptoms are known to result from the occlusion of any of the *exclusively* cerebellar branches. Because of the many anastomoses, softenings of the cerebellum are almost pathological curiosities. The efferent nuclei of the cerebellum are supplied by the superior anterior cerebellar arteries, except for a small part of the nucleus dentatus. The nucleus dentatus is often supplied by a special

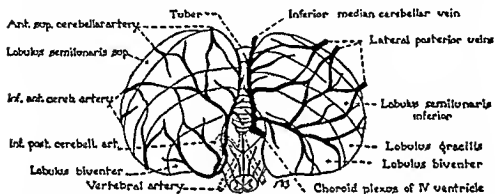


FIG. 15. Scheme of the blood-supply of the surface of the cerebellum exposed by the usual suboccipital exploration. Arteries are represented on the left, and veins on the right hemisphere.

branch and this branch seems peculiarly liable to rupture, forming what is known as the central cerebellar hemorrhage.

The CEREBRAL VEINS (81) may be divided into two systems, the external and internal veins, which have but negligible communications between them with the exception of rare direct communicating channels known as "rod-veins."

The external veins form a network in the pia mater, with many anastomoses, and often the insufficiency of one trunk is compensated by the hypertrophy of another. Nevertheless certain definite groups of venous channels may always be discerned as follows (Fig. 16):

1. The *superior cerebral veins* drain an area above a horizontal line running through the upper part of the sylvian fissure on the lateral surface and on the mesial surface above the callosomarginal sulcus. They arise as innumerable small channels in the cerebral substance

INTRACRANIAL TUMORS

which collect either in the sulci or over the convexity of the convolutions to form larger trunks. The latter pass across directly to the superior longitudinal sinus without any attempt to accommodate themselves to the sulci. There may be from six to a dozen of these vessels, but

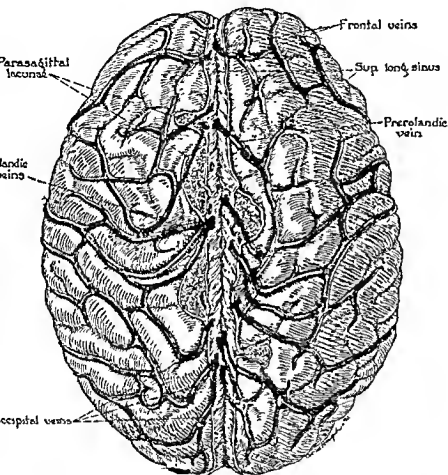


FIG. 16. Superior surface of the cerebrum showing the superior cerebral veins. The superior longitudinal sinus and its lateral lacunae have been left in place.

usually only four or five main trunks are visible. The arrangement on the two sides is often asymmetrical and often a separation into an anterior and posterior group is evident, with a space of four or five centimeters between. The anterior veins are smaller and enter the su-

perior longitudinal sinus practically at a right angle into its lateral wall. They drain the upper parts of the frontal lobes. The posterior group is composed of larger veins of which the most important channels drain the central region. They are directed toward the sinus as long as they remain in the pia mater but, upon emerging from it, curve sharply to run forward, sometimes as much as two or more centimeters, before entering the sinus at its lower angle; the posterior ones may even run in the falx. No veins enter the superior longitudinal sinus in its most posterior portion. There is a tendency, more marked in the embryo, for each external vein to have a corresponding vein on the mesial surface of the hemisphere. The two veins come into contact at the junction of the convexity and interhemispheric fissure, but rarely unite until just before perforating the wall of the sinus. They usually lie together in one sheath but may penetrate into the sinus separately. The point at which these veins pass over from the pia to the dura mater is some distance from their entry into the sinus. That of the anterior veins is obviously from one to four centimeters distant. That of the posterior veins lies much nearer the falx but, since the veins run forward some centimeters, the actual distance from the opening in the sinus is about the same. It is to be noted also that *the veins may lie for a centimeter free in the subarachnoid space while passing from the pia to the dura mater.* They may be adherent to the under surfaces of the dural lacunae but do not empty into them.

2. The *inferior cerebral veins* drain the lower part of the external surface of the hemisphere (Fig. 18). There are two main groups, the lateral occipital and the middle cerebral veins. The lateral occipital veins are formed by some small trunks from the inferior and lateral surfaces of the occipital lobe and more important channels from the posterior part of the temporal lobe, the chief one passing down from the posterior extremity of the lateral fissure. These sometimes unite into a single trunk. At any rate they empty into the middle portion of the transverse sinus, after a short course in the tentorium cerebelli. The other veins converge toward one or two trunks, known as the middle cerebral vein, directed along the lateral fissure forward and downward. In case there are two veins the anterior receives the superficial branches from the anterior external surface of the frontal lobe while the posterior receives those from the anterior portion of the temporal lobe. The middle cerebral vein may curve backward on the under surface of the temporal lobe to end in the superior petrosal sinus but it usually passes

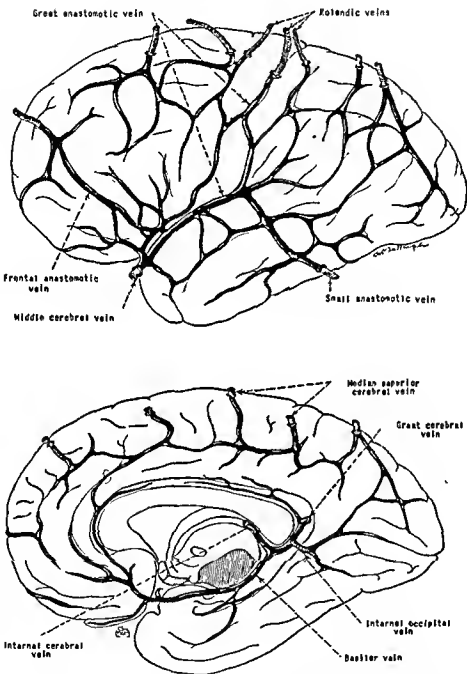


FIG. 17. Scheme of the venous drainage of the cerebral cortex—above, the lateral surface; below, the median surface.

over to the dura mater at the lesser wing of the sphenoid bone to continue as a sinus across the depths of the temporal fossa, entering the superior petrosal sinus after anastomosing in its transit with the middle meningeal veins. It may also empty into the cavernous sinus either directly or via the sphenoparietal sinus.

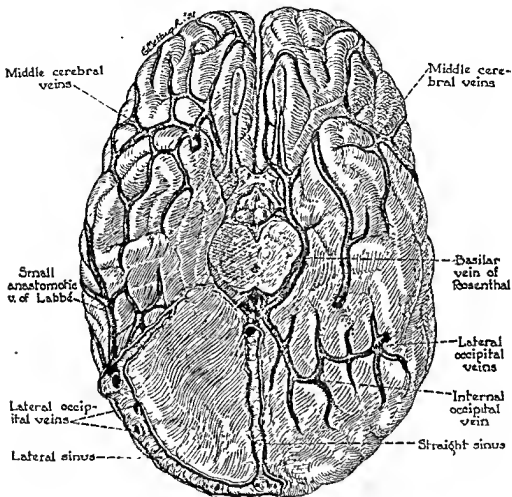


FIG. 18. Inferior surface of the cerebrum showing the cerebral veins.

The venous blood from the anterior part of the corpus callosum and the cingular gyrus drains through an irregular venous channel (Fig. 17) around the knee of the callosal body in the general direction of the anterior cerebral artery toward the base of the brain where it

is joined in the neighborhood of the anterior perforated space by the vein of the lateral fissure, draining the region of the island, to form the *basilar vein* (of Rosenthal). This vein receives many branches from the perforated space, the inferior surface of the frontal lobe, the olfactory groove, chiasm, hypophysis, cerebral peduncle, inferior horn of the lateral ventricle, etc., as it passes backward along the cerebral peduncle and then curves backward and upward around the brainstem in the direction of the quadrigeminal bodies to empty into the internal cerebral vein (Fig. 17). The latter is one of the two large veins which unite to form the great cerebral vein (of Galen). Into the terminal portion of the basilar vein or into the internal cerebral vein drains the important internal occipital vein from the striate area.

The tributaries of all these veins form a network over the surface of the hemispheres, with numerous anastomoses. They seem to radiate from the posterior part of the lateral fissure. Often a large trunk may be seen to run upward from this region to the superior longitudinal sinus, vaguely in the direction of the central sulcus; this trunk, together with the middle cerebral vein, is known as the *great anastomatic vein* (of Trolard). Another large anastomosis may often be seen running backward and downward from the middle cerebral vein to empty into the transverse sinus. It is called the *small anastomatic vein* (of Labbé). Another less-developed trunk runs forward and upward toward the anterior group of superior cerebral veins (Fig. 17).

The *great cerebral vein* (of Galen) drains the internal portions of the cerebrum. It is clearly figured in almost any treatise on the gross structure of the brain.

Some mention might be made of the *superficial veins of the cerebellum*. The lateral posterior veins of the cerebellum empty into the undersurface of the transverse sinus near its middle, or farther laterally. They drain the adjacent tentorial and suboccipital surfaces of the cerebellar hemispheres. The region of the flocculus is drained by many small channels which unite to form the *petrous vein* (or veins), emptying into the superior or inferior petrous sinus. This vein receives also branches of variable importance from the lateral parts of the hemisphere, an important trunk from the interior which drains the dentate nucleus, and also small branches from the pons. The medial part of the superior or tentorial surface of the cerebellum is drained by the superior median veins. They empty usually into the main tributaries of the great cerebral vein (of Galen), occasionally directly into the lat-

ter. The inferior median vein connects upward in the posterior fissure of the cerebellum with the transverse sinus near the torcular (of Herophilus), and downward with the choroid plexuses of the fourth ventricle (Fig. 15).

Not only is it necessary to be able to recognize the gross subdivisions of the cerebral and cerebellar cortex, but one must have some

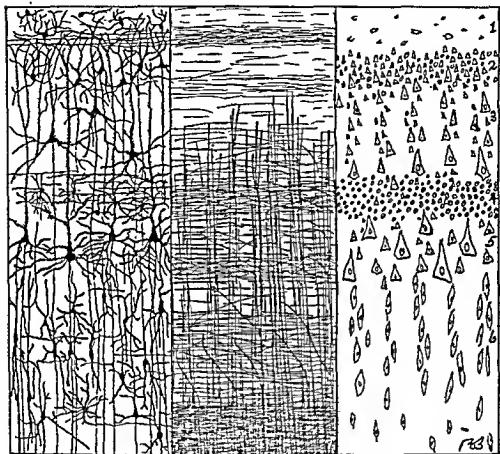


FIG. 19. Diagram of the layers of the cerebral cortex. Left—Golgi's method; middle — Weigert's method; right — Nissl's method.

familiarity with the microscopical structure of the cerebral cortex which has been found to vary widely in different regions (179). When the regions of uniform structure are outlined on the surface of the cerebrum they are found to be quite different from the gross patterns formed by the gyri. Knowledge of CEREBRAL CYTOARCHITECTONICS is important, because evidence is accumulating to show that the variation in structure has a functional significance.

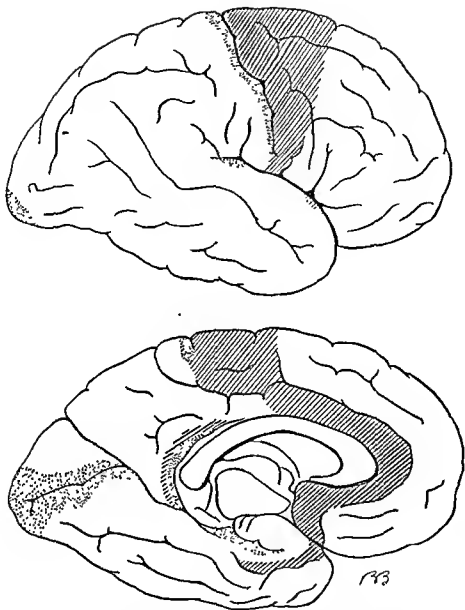


FIG. 20. Scheme of distribution of the granular (stippled) and agranular (cross-hatched) cortex. Compare Fig. 29.

In the greater part of the cerebral cortex the nervous cells form six more or less distinct layers. Even in areas where it is no longer so in the adult, during a certain period of embryonic life at least the six layers are clearly distinguishable. But a small part of the cortex has a barely perceptible or absent stratification, and this non-stratified part is found to occupy a narrow zone extending from the anterior perforated space over the corpus callosum and around the brainstem to the uncus. This narrow, almost completely hidden, band is all that remains in the human brain of the extensive rhinencephalon of lower vertebrates. Its cortical portions are known as the *allocortex*.

The remainder of the cortex, showing either in embryonic or adult life the characteristic stratification into six layers, is called the *isocortex*. Its layers are distinguished as follows from without, inward (Fig. 19):

1. The outermost layer is the molecular or plexiform layer. It contains a great number of dendrites and axis-cylinders of deeper lying cells forming a plexus. There are a number of fusiform cells directed tangentially and known as cells of Cajal.

2. The second layer is the external granular layer composed of numerous closely packed small round cells with scanty cytoplasm.

3. Immediately beneath is a clearer zone composed of more widely scattered and larger cells of pyramidal shape. It is the external pyramidal layer.

4. The fourth layer is again a densely packed area composed of small rounded granular cells, the internal granular layer.

5. The fifth layer consists again of large scattered pyramidal cells. It is the internal pyramidal layer.

6. The sixth layer is composed of more spindle-shaped cells which have their long axes directed perpendicularly to the surface of the brain. They are smaller than the pyramidal cells and are divided roughly into columns by the axis-cylinders of the overlying pyramidal cells.

While these six layers may be distinguished, at one time or another, throughout the isocortex, yet in the adult they are obscured in certain regions of the adult brain by two modifications—either by increase in number of the grains, or of the pyramidal cells. The first modification results in what is known as the *koniocortex* in which the granular cells invade especially the third layer, but also the fifth and sixth. This type of cortex is found on the posterior lip of the central sulcus, on both sides of the calcarine fissure, on the deep transverse

temporal convolution, on the interior lip of the fissure of the callosal body and of the hippocampal fissure (Fig. 20). The other modification results from a great increase of the pyramidal cells with a corresponding decrease in granular cells, so that the internal and external granular layers tend to disappear. This type of *agranular cortex* covers the posterior third of the frontal lobe on both its external and internal surfaces, and also the anterior part of the limbic convolution and the parolfactory area (of Broca). There are also small agranular areas in the retrosplenial segment of the limbic convolution and parts of the hippocampal and uncinate convolutions (Fig. 20). In general injuries to the granular or agranular cortices are attended by striking symptoms (p. 61 ff.).

In all the rest of the adult isocortex the six layers may be more or less clearly distinguished, yet its structure is far from uniform. More

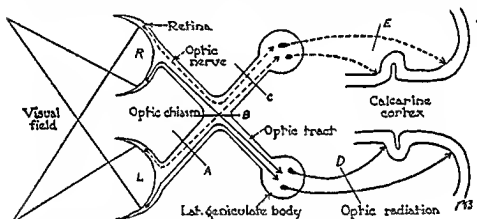


FIG. 21. Scheme of the visual pathways showing effects of various lesions. A—complete blindness of left eye; B—bitemporal hemianopia; C—left homonymous hemianopia; D—right homonymous hemianopia; E—left homonymous defect in visual fields (See also FIG. 29.)

than a hundred distinct structural areas may be isolated. A discussion of them would take us too far afield. Suffice it for our present purposes to remark that three principal types may be distinguished. The *parietal type* is not definitely stratified. The internal and external granular layers are especially distinct, and its pyramidal cells are rather small. The *frontal type* is definitely stratified but its granular layers are not very thick and their cells tend to be triangular. Its pyramidal cells are larger and more numerous. The *polar type* is distinguished by its narrowness and the density of its cells, which make its stratification

very obvious. These three last types make up the greater part of the cortex as will be apparent from a glance at Figure 20. These types cover vast areas whose destruction causes often no very obvious symptoms so that they are sometimes referred to as "silent" areas.

Within the cortex lie the intricate networks of the *fiber-tracts* which the anatomists of the last generation, by the use of the methods of Weigert and Marchi, worked out in great detail. The results of their investigations are described in all textbooks of neurology, and a knowledge of them is essential for the understanding of the symptomatology of intracranial tumors. The symptoms resulting from their interruption have preoccupied neurologists for decades. It is impossible for us here to give even a brief summary of the fiber-tracts in the brain. We will take time only for a description of the VISUAL SYSTEM which stretches the entire length of the brain. Few are the intracranial tumors which do not involve it either directly or indirectly.

The image of the external world, or visual field, for purposes of description may be divided into four quadrants. The internal structure of the eyeball is such that the lower right quadrant of the visual field is projected on the upper left quadrant of each retina, and similarly the upper right quadrant of the external world on the lower left quadrant of each retina. There is a similar relationship of the left visual field with the right portions of the retinas (Fig. 21). From the retinas the visual impulses are carried by the optic nerves to the chiasm where a rearrangement occurs. The fibers carrying impulses from the left half of each retina pass into the left optic tract, while the fibers from the right half of each retina pass into the right optic tract. In other words, only the fibers from the nasal half of each retina cross in the optic chiasm. In the postchiasmal optic tracts, which end in the external geniculate bodies, the crossed fibers lie ventromesially and the uncrossed dorsolaterally.

Thus far their course has long been known, but the exact relationships of the fibers beyond the geniculate bodies have only recently been elucidated and cannot still be considered as completely known (306). Essentially their course seems to be as follows. The fibers from the upper quadrants of the retinas end in the mesial horns of the geniculate bodies and those from the lower quadrants in the lateral horns. In the geniculate bodies new neurones carry the impulses outward, those arising in the mesial horn pass outward and then curve backward in a long arch around the ventricle to end in the striate area

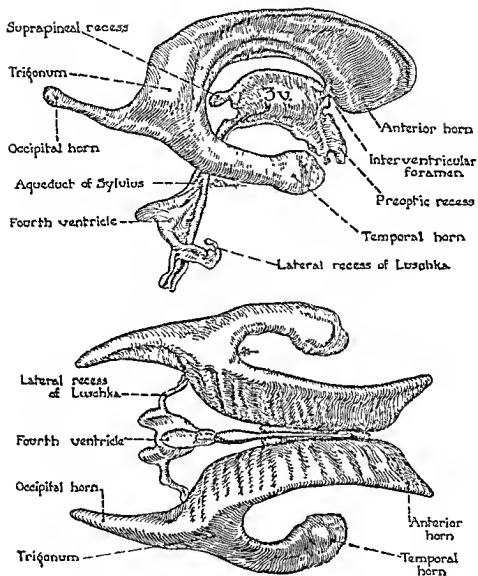


FIG. 22. Casts of the ventricular system—above, superior view; below, lateral view (after Retzius).

on the upper lip of the calcarine fissure. Those arising from the lateral horn of the geniculate body form *a long loop anteriorly toward the tip of the temporal lobe* (389), then curve around the temporal horn of the lateral ventricle to run in the inferior longitudinal bundle and end on the lower lip of the calcarine fissure. The most superior and inferior fibers in the radiation end at the anterior extremity of the calcarine fissure (386); those lying between end more posteriorly (Fig. 29). There is evidence also that the sections of the retina along the horizontal meridian send their fibers to end in the depths of the calcarine fissure, whereas those sections along the vertical meridian send their impulses to the lips of the fissure and the external surface of the hemisphere (261). The fibers of the optic radiation are so widely spread apart in the temporal lobe that it is possible for even large lesions to cause only a partial interruption producing what are known as homonymous quadrantic defects in the visual fields.

The foregoing relationships hold for the greater part of the binocular visual field. But the course of the macular impulses is not so definitely known. In the optic nerve the macular bundle near the bulb occupies the lateral side of the optic nerve and gradually shifts to a median position as the chiasm is approached (490). It consists of a crossed and uncrossed portion. The crossed fibers pass through the posterior border of the optic chiasm. In the optic tract these fibers again lie in the center of the tract. In the external geniculate body the macular fibers probably end between the quadrantal fibers in the upper portion of its posterior half. From here the impulses are conducted in the geniculostriate projection *between the upper and lower quadrantal fibers* to end certainly in a wedge-shaped portion of the striate area at the tip of the occipital pole. The macula has been thought by some investigators to be bilaterally represented in the occipital cortices, but this view has not been established and in all probability is erroneous. These relationships are shown graphically in the accompanying illustration (Fig. 29).

Within all the myriad of intricate fiber-systems we find the brain to be hollow, for it develops from the simple neural tube. But the simple cavity of the tube becomes in the adult brain very complicated and a knowledge of its relationships we will find to be of great importance for the study of intracranial tumors. It has in the adult a series of enlargements called VENTRICLES united by narrow passages. In each cerebral hemisphere lies a *lateral ventricle*, having three horns

meeting in the parietal region in an enlarged portion called the trigonum collaterale. The anterior horn is deeply indented on its lateral surface by the head of the caudate nucleus (Fig. 22). The temporal horn is smaller and narrower and extends into the temporal lobe. The occipital horn, which projects backward into the occipital lobe, is very inconstant in size and length. The anterior horns lie very close together in their middle and posterior portions, being separated only by the thin septum lucidum; they diverge somewhat at their anterior extremities. The occipital horns are somewhat widely separated, while the temporal horns diverge still more markedly from each other. Most representations of the lateral ventricles show them grossly dilated by the injection-mixture used to make the cast from which the illustrations

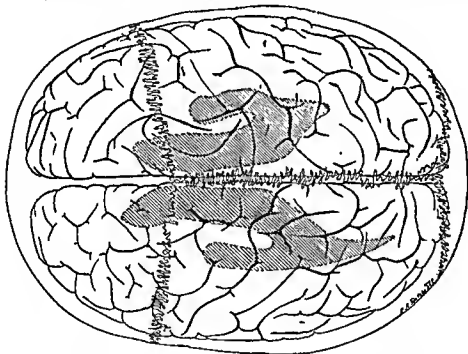


FIG. 23. Projection of the lateral ventricles on the superior surface of the brain and cranium (from Spitzka).

are taken. They are normally quite narrow except for the trigonum. There is often considerable asymmetry of the two lateral ventricles (Fig. 23).

The lateral ventricles communicate through small apertures called *interventricular foramina* (of Monro), with a single median cavity, or

third ventricle, which lies between the optic thalami. It is very narrow; in fact the two thalami usually come together and fuse in its median portion to form the intermediate mass. The third ventricle in its turn communicates posteriorly by a long narrow *aqueduct* (of Sylvius) through the midbrain with a *fourth ventricle* lying between the bulb and the cerebellum. The fourth ventricle in the embryo continues down the spinal cord as the central canal. In the adult this canal is practically obliterated.

The walls of the neural tube in the adult become attenuated and finally break down at three points, one in the median dorsal line at the posterior extremity of the fourth ventricle (*foramen of Magendie*) and laterally near the flocculi of the cerebellum (*foramina of Luschka*) so that the ventricular system at these points is in direct communication with the subarachnoid space. The walls of the lateral ventricles are also very thin and easily ruptured along the fimbriae hippocampi.

The cerebral ventricles are filled with the same colorless fluid which is present in the subarachnoid space. The fluid seems to be formed mainly by vascular CHOROID PLEXUSES which lie in the roof of the third and fourth ventricles and in the mesial walls of the temporal and frontal horns of the lateral ventricles. This fluid plays a major rôle in the symptomatology of intracranial tumors. In the human being the cerebral ventricles can be made visible by replacing the fluid with air, which casts a shadow on the x-ray plate. This process is known as ventriculography (cf. p. 422).

We have now reached the center of the head, noticing on our way only a few of the most important structures. But we must say a final word about the PINEAL BODY, a tiny out-pocketing of the roof of the diencephalon, which in lower vertebrates is a median eye. In the human being it is a vestigial structure which interests us largely because it is often calcified and so casts a shadow in roentgenograms. Since it lies exactly in the median plane of the head, the shifting of this shadow to right or left helps occasionally to determine on which side a tumor lies (357). What a comedown for a structure formerly supposed to be the seat of the soul!

These brief notes on the structure of the cranium and of its contents are little more than indications of certain things which I consider it important for the student to learn. They will be supplemented as we go along and *the student should never forget that he must be able to visualize the intracranial structures in their most minute details if he is to understand adequately the symptomatology of intracranial tumors.*

CHAPTER 3

ELEMENTS OF CEREBRAL PHYSIOLOGY

Knowledge of the functions of the various structures within the intracranial cavity is no less important than that of their form and relationships because *the diagnosis and localization of intracranial tumors is principally made from deranged function.*

As one opens into the intracranial cavity he comes soon upon the clear and colorless cerebrospinal fluid which everywhere surrounds the central nervous system within the meshes of the pia-arachnoid membrane. The brain and spinal cord are practically suspended within this liquid medium, which must act as a buffer to protect it from shocks. It is not known that the cerebrospinal fluid has any special function, although some have thought that waste-products of the nervous tissue are discharged into it by way of the perivascular sheaths. The fluid is interesting to us largely because of its circulation.

The CEREBROSPINAL FLUID is produced by filtration from the blood (212) chiefly through the semipermeable membranes formed by the choroidal plexuses in the walls of the ventricles. As in the case of the aqueous humor of the eye and the glomerular fluid in the kidney it is practically free of proteins and has a high chloride-content which keeps it in osmotic equilibrium with the bloodplasma (213). The protein-content of the fluid in the lumbar region is 30 mgm. per 100 cc., in the cisternal region 25 mgm. per 100 cc., and in the ventricles 10 mgm. (13). The content in chlorides is 720-750 mgm. per 100 cc., considerably higher than the content of bloodplasma.

The pressure at which the fluid is filtered through the capillaries of the plexuses is equal to the pressure in the capillaries minus the osmotic pressure of the nonpermeable constituents of the plasma. The actual pressure in the ventricles is always lower because of continuous absorption. In accordance with these facts the rate of formation and pressure of the cerebrospinal fluid may be increased, among other methods, by decreasing the osmotic pressure of the plasma, or by increasing the pressure in the capillaries. The former may be done by intravenous injection of distilled water and the latter by occlusion of the great cerebral vein (of Galen) (458). Conversely by injection of hypertonic

solutions into the venous system the pressure of the cerebrospinal fluid may be made to fall rapidly (504) to zero, even reversing its flow through the choroidal plexus.

The actual normal pressure of the cerebrospinal fluid, with the subject in the horizontal position, varies from 100-200 mm. of water (503). With the subject in the sitting posture the pressure of the fluid

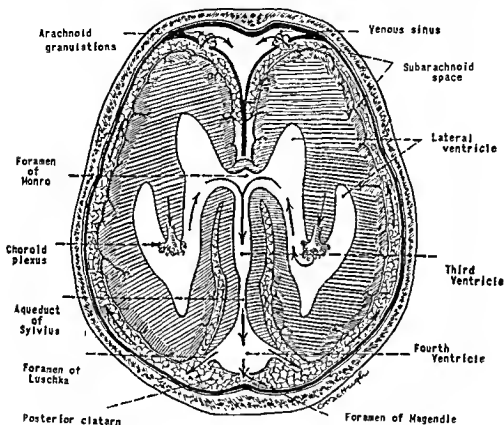


FIG. 24. Diagram of the circulation of the cerebrospinal fluid.

in the ventricles is zero or even less, while in the lumbar region its pressure depends upon the hydrostatic pressure of the fluid above the level measured. The pressure of the fluid is influenced, aside from the osmotic pressure of the blood, by both the arterial and venous pressure, but follows the latter more closely (62). It is usually slightly higher than the venous pressure. The actual pressure of the cerebrospinal fluid when the subject is in the horizontal position is the same all along the subarachnoid space, and when the pressure is increased at any

point, it is instantaneously increased in all parts of the subarachnoid space. Since the pressure follows closely the intracranial venous pressure *it is very easy to raise the pressure of the cerebrospinal fluid by obstructing the internal jugular veins in the neck*, thus causing an intracranial venous congestion (Queckenstedt's test).

Most of the fluid is formed in the lateral ventricles and passes from there through the interventricular foramina to the third ventricle, then through the aqueduct (of Sylvius) into the fourth ventricle, whence it passes through the median foramen (of Magendie), and the lateral foramina (of Luschka) into the posterior and basilar cisterns of the subarachnoid spaces (Fig. 24). This flow cannot be observed directly but is inferred from both clinical and experimental evidence which shows that an obstruction of the median and lateral foramina causes a hydrocephalus of the entire ventricular system, while an occlusion of the aqueduct causes dilatation only of the third and lateral ventricles (156). Moreover, an obstruction of one interventricular foramen causes distension only of the corresponding lateral ventricle; if the choroidal plexus of this ventricle be previously removed no distension results (155).

Similarly it has been shown that from the basilar and posterior cisterns the fluid passes mainly upward around the brainstem over the cerebral hemispheres to be absorbed into the venous lacunae of the dura mater through the arachnoidal granulations (501). These granulations are most abundant along the superior longitudinal sinus. If they be occluded a hydrocephalus also develops (500) and, if dense adhesions are formed around the brainstem, the same result follows (155).

The choroidal plexuses are not the only sources of the cerebrospinal fluid nor are the arachnoidal granulations the only sites of its absorption. If the spinal canal be blocked and the fluid removed from below the obstruction, the fluid is soon reformed. And, at least in certain animals, if the arachnoidal granulations are separated from the dura mater the fluid is still properly absorbed. It is probable that the fluid may be formed by direct transudation through the walls of the capillaries in the pia-arachnoid membrane, and that it may be reabsorbed by the same capillaries, especially over the sulci and gyri of the cerebral hemispheres. It has been shown also that part of the fluid is absorbed along the nerves which leave the cranial and spinal cavities (499).

It should be noted how many narrow passages occur along the

course of this fluid, so that its flow is readily blocked. The result is that disturbances of the circulation of the cerebrospinal fluid play an enormous rôle in the symptomatology of intracranial tumors. If the fluid is prevented from reaching the venous sinuses, the pressure of the fluid tends to approach the diastolic arterial pressure. Formation of fluid would then stop were it not for the fact that the veins of the plexus are compressed. This causes the capillary pressure to rise and filtration starts again and a vicious circle is set up until the highest possible capillary pressure is reached, somewhere near the diastolic arterial pressure. Since little, if any, fluid is absorbed in the ventricles, the constant high pressure causes dilatation of the ventricles and a hydrocephalus develops. If the obstruction is near the aqueduct the process may be aggravated by compression of the great cerebral vein (of Galen) which would also tend to raise the capillary pressure in the plexuses.

The volume and rate of the VASCULAR CIRCULATION through the brain depend on two factors, (1) the caliber of the intracranial arterioles and capillaries and (2) the difference between the arterial and venous blood-pressures (200). The caliber of the intracranial arterioles is influenced by chemical substances in the bloodstream, by vasomotor nerves, by variations of the venous pressure and by variations in the pressure of the cerebrospinal fluid. The difference between the arterial and venous pressures is influenced by obstruction to the venous outflow from the intracranial cavity, by variations of the systemic arterial pressure and by variations in pressure of the spinal fluid.

Any increase in the pressure of the cerebrospinal fluid is immediately transmitted to the thin-walled veins, so that pressure of the venous blood and of the cerebrospinal fluid becomes almost identical. The rise in pressure within the veins causes stasis of blood. If the rise in pressure is slow, and not too great, vasodilation results permitting the arterial pressure to be more directly transmitted through the capillaries and arterioles into the veins, thereby overcoming the venous stasis by increasing the venous pressure. The velocity is lowered but the volume is maintained by the vasodilation. If the rise in cerebrospinal pressure is sudden and great, or if the difference between the arterial and venous pressure becomes so small that the velocity is reduced to approximately half the normal, a rise in systemic arterial pressure is necessary to overcome the venous stasis, the difference in arterial and venous pressure increases, and the velocity of the intracranial blood-

flow again approaches the normal (519). This is brought about by a stasis in the vasomotor center of the bulb. This center is very sensitive to increase in the carbon dioxide of the venous blood and its stimulation results in a rise in systemic arterial pressure via the splanchnic nerves. *This rise of systemic arterial pressure following increase of the general intracranial tension is accompanied by slowing of the pulse rate* (Fig. 25), and the combination of the two symptoms is of the utmost importance in the clinic for the diagnosis of increasing intracranial

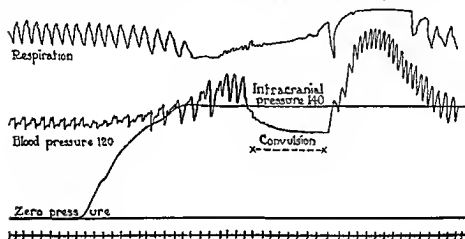


FIG. 25. Result of increasing the intracranial pressure on pulse, blood pressure and respiration (after Cushing).

tension (126). If the tension becomes too great, rhythmical irregularities of respiration occur (Cheyne-Stokes respiration).

Because the veins of the eyeball drain backward into the cranial cavity local obstruction back of the orbits or general increase of intracranial pressure will interfere with their circulation. The result may be seen in the retina by examination with the ophthalmoscope. The veins become engorged and tortuous, the papilla of the optic nerve edematous and swollen (370). *The optic disc is said to be "choked."* If the obstruction continues hemorrhages occur and finally atrophy of the nervous fibers.

But most important for our theme, of course, is an appreciation of the manifold FUNCTIONS OF THE BRAIN. The brain is really a compact group of organs. Our knowledge of their functions at the present time indicates that as the various parts of the brain are not identical in structure so they are not equipotential. This knowledge is largely

inferred from two sources of information, (1) the results of stimulation and (2) the results of destructive lesions of localized portions of the brain. Many inferences are also drawn, (3) from the connections of different parts by way of fiber-tracts (259).

Stimulation of the cerebral cortex is most readily obtained with an electrical current and this experiment has been made numerous times (194) on the brains of conscious patients operated upon under

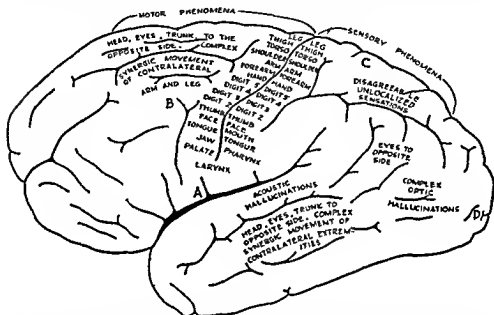


FIG. 26. Results of electrical stimulation of the cerebral cortex. A—chewing, licking, and swallowing movements; B—eyes turned to the opposite side without visual aura; C—sensory aura in opposite leg followed by complex synergistic movements; D—unformed optical phenomena such as flames and lights (after Foerster, modified).

local anesthesia. The results may be rapidly learned from a reference to Figure 26. It will there be seen that the stimulation of the precentral gyrus in a definite order from above downward causes localized muscular movements involving progressively the thigh, trunk, shoulder, hand, fingers, face, and throat. The motor centers for the foot and perineum are on the medial surface of the hemisphere (423). It should be remarked that the size of the area from which movements of the fingers can be elicited is out of all proportion to that of the rest of the motor area. If the stimulus is weak the movement is isolated and can be elicited only from the posterior margin of the anterior central gyrus. If the stimulus be stronger the movement may be obtained from

a wider area but spreads to adjacent parts and may finally involve a half or even the entire body in a convulsive attack exactly resembling the epileptic attacks observed in the clonic. Anterior to the central gyri such convulsive attacks may be precipitated by strong stimulation of the posterior third of the superior frontal convolution. The head, eyes, and trunk bend to the opposite side and tonic complex movements of the contralateral arm and leg follow. Stimulation of the posterior extremity of the middle frontal convolution is similarly followed by isolated turning of the eyes to the opposite side.

Slight stimulation of the anterior margin of the posterior central convolution results in exquisitely localized sensations which follow closely in distribution the movements elicited by stimulation of the anterior central gyrus. With slightly stronger excitation the movement of the corresponding part may accompany the sensation. Back of the posterior central convolution no effect follows very light stimulation but stronger excitation of the anterior extremity of the superior parietal lobule elicits a sensory aura in the opposite arm and leg followed by complex synergistic movements of the contralateral arm and leg. Farther back in the same lobule, stimulation is followed by a turning of the head, eyes, and trunk to the opposite side very similar to that elicited by stimulation of the posterior part of the superior frontal convolution.

Stimulation of the posterior part of the superior temporal gyrus also causes the eyes, head, and trunk to turn to the opposite side but this is now preceded or accompanied by acoustic aura or hallucinations. Excitation of the occipital pole causes epileptic attacks, ushered in by optical aura, such as lights, flames or stars, usually in the opposite visual field. Stimulation farther forward on the occipital lobe causes turning of the eyes to the opposite side associated with formed optical hallucinations.

Much information has also been obtained concerning the functions of the various parts of the brain from the study of the *results of occlusion of arteries*. This information is useful not only to the student of physiology but also to the surgeon who would operate on the brain and who needs to know what is apt to follow the ligation of the branches of the cerebral arteries. The superficial cerebral arteries are not endarteries but their anastomoses are not sufficient to prevent serious degenerations following occlusion of the main trunks. The resulting softening is most complete near the point of obstruction, the more distal parts being saved by anastomotic circulation.

Occlusion of the anterior cerebral artery (113), before the origin of the recurrent branch, results in a severe hemiplegia of spastic type and a left-sided apraxia if the hemiplegia is right-sided, also some motor aphasia if the lesion is left-sided. There is often some sensory impairment in the lower limb. When the hemiplegia is left-sided the apraxia is masked by the paralysis. Some degree of mental loss will be present, comprising retardation, confusion, and disorientation amounting at times to actual dementia. When this artery is occluded after the origin of the recurrent artery (of Heubner) the hemiplegia

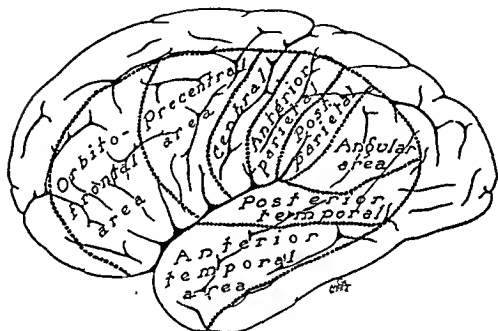


FIG. 27. Scheme of the lateral surface of the cerebrum showing areas of distribution of the branches of the middle cerebral artery.

will predominate in the leg, and is often flaccid; sensory changes are present as before; apraxia is present in the left arm whichever side is affected by the paresis; the mental changes occur as before, and aphasia also, and the phenomenon of forced-grasping occurs in the paretic upper extremity. The resulting softening shows that the absence of a massive hemiplegia is due to the escape of the internal capsule.

The posterior cerebral artery (198) may be still more briefly disposed of. Symptoms which may arise from the occlusion of this artery or its branches are numerous and include hemiplegia, hemianesthesia, hemianopia, aphasia with alexia predominating, cerebellar troubles of

asynetic type, paralysis of the oculomotor nerve and choreoathetosis. But there seem to be abundant anastomoses because softening of the entire area is rare. The peduncular territory in particular usually escapes. When the occlusion lies near the origin of the artery its proximal territory suffers most and there is a hemianesthesia of the thalamic type. Pain and thermal sense are disturbed with spontaneous pain in the affected side; painful stimuli have a peculiar radiating quality and cold in particular has a very disagreeable effect. There may be homolateral asynergia due to involvement of the superior cerebellar peduncle. There may be added a defect of the visual fields and mild aphasia with alexia if the posterior distribution is also softened. Of its three terminal branches the calcarine is most often occluded, giving rise to a hemianopia, with or without alexia depending on the hemisphere affected.

It is concerning the middle cerebral artery that information is most abundant and detailed (197). The cortical areas involved may be seen in Figure 27. Since lesions of the middle cerebral artery result often in difficulties of speech it might be well to stop a moment to determine some of the terminology which we will have to use. It would take too much space to justify the terms used. Suffice it to say that we shall employ the following terms: (1) aphasia, a disturbance of internal language; (2) anarthria, a difficulty in externalizing speech in the absence of paresis of the peripheral mechanism; (3) dysarthria, a difficulty in externalizing speech due to paresis of the peripheral mechanism; (4) alexia, difficulty in understanding written language; (5) auditory verbal agnosia, difficulty in understanding spoken language with intact peripheral mechanism; and (6) apraxia, difficulty in the execution of skilled acts (other than speech) in the absence of paralysis, sensory loss, or incoordination of the limbs. Three types of apraxia will be distinguished: (1) motor apraxia, which affects only the left arm and is due presumably to inability to transmit voluntary impulses to the right motor cortex; (2) ideational apraxia, due to loss of the conception of the act to be performed; and (3) ideomotor apraxia, a mixture of the two which predominates usually in the right hand.

Complete softening of the territory of the middle cerebral artery, from occlusion at its origin, is hardly compatible with life. Such patients are comatose and survive but a short time. It is possible to determine, however, that there is a gross hemiplegia, hemianesthesia, hemianopia and, if the lesion is on the left side, a complete aphasia. Usually, however, a great part of the superficial distribution of the

artery escapes, due to collateral circulation, so that the most profound destruction occurs in the region of the perforating arteries and the proximal part of the superficial distribution, especially the island. The symptoms in this case are an intense hemiplegia, as marked in the lower as in the upper extremity. Secondary contracture is apt to be absent, the hemiplegia remaining flaccid with slight exaggeration of the reflexes. Sensory troubles when they exist are very slight. There may be a hemianopia. When the lesion is on the left side an aphasia is present with anarthria predominating. When the lesion is confined to the perforating branches there is an ordinary hemiplegia, except that the leg is usually as much involved as the arm, with contractures, exaggerated reflexes, clonus and extensor plantar response. Sensory troubles are practically absent and there is no hemianopia. There is also no aphasia.

If we turn now for a moment to study the effects of occlusion of the terminal branches of the superficial distribution, we find that isolated cases of occlusion of the orbitofrontal, posterior parietal, rolandic, angular, and anterior temporal arteries are rare and incompletely reported. It would seem that occlusion of the posterior parietal branch causes astereognosis and some loss of sense of position in the opposite arm and, if on the left side, an ideomotor apraxia. Occlusion of the posterior temporal artery, especially if it is well-developed, causes a hemianopia (and aphasia if the lesion be left-sided) with an ideational apraxia. The artery of the angular gyrus causes an alexia with some defect in the visual fields. The isolated occlusion of the prerolandic and interparietal arteries is more common. Occlusion of the prerolandic artery gives rise to a contralateral facial weakness, deviation of the tongue and weakness of the masticatory muscles, the upper and lower extremities being usually intact. When the lesion is on the left side there is added an anarthria, with aphasic troubles dominated by an intense alexia without hemianopia. The anterior parietal artery causes a hemiparesis, the movements of the hand being somewhat unstable and irregular and the lower limb a little trembly and hesitant. There is a hemihyesthesia involving all modes of deep and superficial sensation. There is no hemianopia and pyramidal symptoms are slight. At times the arm is much more profoundly paretic and, if the lesion is left-sided, an ideomotor apraxia may be present.

Occlusion of two branches at a time is frequent. The posterior temporal and the artery of the angular gyrus are often simultaneously

occluded. When such a lesion affects the right hemisphere there is simply a hemianopia. When the left hemisphere is affected there is a marked aphasia; the amnesia is profound, involving loss of vocabulary, calculation, complex acts, and even such simple acts as are used in testing for ideational apraxia. Occlusion of the posterior parietal and angular arteries together is also common. Hemianopia results always. In the left hemisphere is added also a moderate aphasia and ideomotor apraxia. Spatial representation is disturbed, and the execution of acts. Often sense of position is much disturbed, and errors in localization are gross.

The softening resulting from occlusion of the rolandic artery varies greatly in extent. At times the lower end of the central fissure is supplied by a branch of the prerolandic artery and again the upper end by a branch of the anterior parietal artery. The most upper part of the precentral gyrus is always supplied by the anterior cerebral artery. Occlusion of the rolandic artery leaves the lower end of the anterior central convolution intact and also the lenticular region. Hemianesthesia predominates without aphasia or anarthria; there is a hemiparesis with the intensity and distribution of the paralysis very variable.

Obstruction of the middle cerebral trunk usually occurs after the origin of the anterior temporal artery. When the obstruction lies anterior to the common ascending trunk the hemiplegia is outstanding, with both aphasia and anarthria. The absence of hemianopia when the lesion is far forward is due to the fact that the softening of the posterior part of the distribution of the middle cerebral artery is not complete because of the collateral circulation. The hemiplegia and hemianesthesia predominate definitely in the arm. There is a lower facial weakness but almost always no loss of sensation over the face, and the leg also may escape an anesthesia. Anarthria is more common and aphasia may be slight. When the obstruction lies beyond the origin of the ascending trunk, the hemiplegia is slight or absent but hemianopia is practically constant; in the left hemisphere an intense aphasia and apraxia also result.

In general the results of *occlusion of the superficial cerebral veins* are not very well known. One notable exception is the group of precentral veins (486). Ligature of the superior longitudinal sinus back of them causes a paresis of both lower extremities, most marked in the distal segments (267). There is a severe rigidity with exaggeration of the tendon-jerks and extensor plantar responses and sometimes loss of

postural sense in the legs. The legs are usually extended, adducted and rotated inward, the great toes being dorsally flexed. Similar effects in the contralateral leg follow ligation of these veins only on one side. Occlusion of the left middle cerebral vein usually causes an aphasia and weakness of the facial muscles which slowly improve. Occlusion of the small anastomotic vein of Labbé may have similar effects. The obstruction of the great cerebral vein (of Galen), which has few anastomoses with the superficial veins, causes coma with hyperpyrexia, elevation of the pulse and respiratory rate, contraction of the pupils, rigidity of the limbs, and exaggeration of the tendon-reflexes (16). More chronic obstruction to this vein seems to cause a mild internal hydrocephalus (458). Occlusion of the internal occipital vein seems to result in a hemianopia which may be permanent (244).

If we turn now to the effects of *direct injury to the cortex* we will find that its results agree in a general way with those of electrical stimulation and of softenings. The World War was a veritable experimental laboratory for the study of the physiology of the brain (270), and much of our knowledge has been obtained from the study of wounds received in this conflict.

We may begin with lesions in the territory of the frontal pole. (190). They have been held responsible for a long series of troubles, prominent among which are disturbances of character. A patient with an injury in this region is inattentive, his time of comprehension is lengthened, new facts are appreciated with difficulty. He seems unable to grasp a situation as a whole. The emotional life is disturbed; such patients cry or laugh easily. Self-control seems poor. Ill humor, sexual lapses, depression, hysteroid attacks are common. Prominent is a tendency to "wisecracking." Lack of orientation to the social and ethical restraints of the group, torpor, slowness in the formulation of ideas, marked irritability, and gross disorientation as to space and time are described. Injury to the posterior part of the superior frontal convolution causes a symptom known as "forced grasping" (1) in which the fingers close over any object placed in the hand and the patient cannot voluntarily relax his grasp. Inability to relax all the muscles of one side may be seen. Disturbance in conjugate movements of the head and eyes is frequent. The motor reaction-time is lengthened. The opposite labyrinth is overexcitable. Visual nystagmus to the side opposite the lesion may be absent.

The correlation of these symptoms with the architectonics of the

frontal region of the brain is at present impossible. The neurologist is often not interested in the psyche, and the psychiatrist of today is also not often interested in the structure of the brain. The result is that these patients fall between Scylla and Carybdis. Many of them die in asylums where no one is interested in studying their brains and when a brain falls into the hands of a neuroanatomist he usually finds that the clinical observation leaves much to be desired. There is, however, some evidence to relate the tonic innervation and forced grasping to

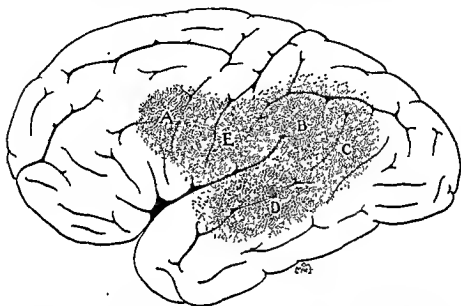


FIG. 28. Scheme of the main aphasic zone of the left cerebral hemisphere, as indicated by the effects of war-wounds (after Foix). Interpreted in text, page 65.

lesions of the posterior extremity of the superior frontal convolution. The loss of optic nystagmus is related to the posterior extremity of the middle frontal gyrus. The disturbances of intellect, emotion and character cannot be sharply related to any particular area of the frontal lobes; they seem to be more pronounced in injuries to the left frontal lobe. With injuries to both frontal lobes these psychic changes become profound (79).

If we move now to the opposite pole of the brain the study of war-wounds has made it evident that injuries in the region of the calcarine fissure cause defects in the visual fields (266) and the analysis has been carried so far that we now know that lesions of the upper part

of the calcarine area cause an inferior quadrantic hemianopia. Complete destruction of one calcarine area causes homonymous hemianopia. Lesions of the tip of the occipital lobe and of the posterior part of the calcarine fissure cause loss of macular vision. It seems perfectly evident that there is a point-to-point projection of the retina on the calcarine region. Lesions of the outer surface of the occipital lobe are sometimes associated with disturbances of movements of the eyes and loss of spatial orientation, so that the patient loses his way in familiar surroundings (265). When the lesion approaches the supramarginal gyrus there is added difficulty in estimating distance and failure to recognize relative lengths and sizes of objects. There is also great difficulty in fixation of objects and in convergence and accommodation. Patients may collide with objects although seeing them. Injury to the left angular gyrus causes alexia; nearby lesions agnosia for fingers.

In the temporal lobe we find that a lesion almost anywhere, if it involves the subjacent white matter, will cause a homonymous defect in the visual fields (133). A glance at Figure 29 will show why this must be so; the fibers of the optic radiation make a long curve forward around the temporal horn of the lateral ventricle thus exposing themselves to injury over a long distance. There is little evidence that a unilateral lesion of the temporal lobe will cause defect of hearing but a bilateral lesion has been described which resulted in deafness (349). This lesion involved on both sides the posterior thirds of the superior temporal gyri, the transverse gyri, and the posterior parts of the middle temporal gyri. There is no known case of bilateral destruction of the transverse temporal gyri without serious defect of hearing.

Injuries of the anterior central gyrus cause paralysis, and the distribution of the paralyses corresponds with the results of electrical stimulation (67). Injuries to the upper part cause paralyses of the lower limb, and to the lowest part paralysis of the face and throat. The areas for the arm and trunk lie in the middle region. These palsies may be sharply localized; paralyses restricted to two adjacent fingers have been observed.

Wounds of the posterior central gyrus have shown no such sharp localization but in a grosser way a similar distribution exists (67), in that injuries of its upper end cause sensory loss over the leg and foot, while injuries to the lower end cause loss over the face. The arm and hand occupy a large intermediate zone, the ulnar area lying above the radial. The distal parts of the limbs are more affected than the proxi-

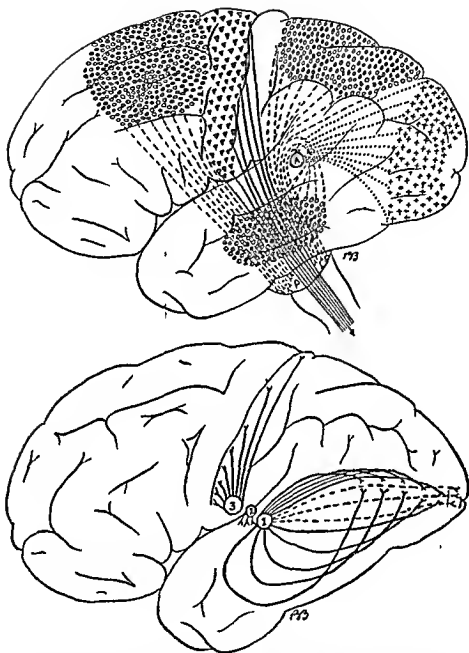


FIG. 29. Scheme of the main projection-pathways of the cerebral cortex—above, the efferent pathways with the origin of the cerebropontine tracts indicated by circles, the origin of the cerebrospinal tracts by triangles and the visual efferent pathways by crosses; below, the afferent pathways with the macular projection indicated by dashes. A—anterior quadrigeminat body; 1—lateral geniculate body; 2—medial geniculate body; 3—thalamic nuclei; P—pons. The exact origin of the cerebropontine pathways is disputed.

mal parts. The somesthetic cortex is widely spread in the parietal area and covers the postcentral gyrus, the superior parietal lobule, and part of the supramarginal gyrus. Injuries within these regions cause sensory loss of a peculiar type on the opposite side of the body (249). The crude recognition of touch, pain, temperature, and pressure is retained. The recognition of posture, the distinction of form and the discrimination of compass-points are those elements in which disturbance can be most frequently observed and most readily demonstrated. As a general rule in pure cortical lesions those forms of sensation subserved by the deep afferents, and consequently those which give us information as to the position in space of parts of our body, the spatial relations of different parts of our limbs and of their movements as well as the power of recognizing the shape of objects by handling them and their weight, are more affected than cutaneous sensibility. Defective recognition of differences in weight is most often present but is not so easily tested in the clinic. Next in order comes disturbance of appreciation of position and of movement and of the compass-test. The exact localization of destructions causing loss of various aspects of sensation is disputed. The sense of position seems to be heavily represented in the posterior central gyrus. Tactile impairment possibly is more affected in a horizontal zone running across the foot of the posterior central gyrus and the supramarginal gyrus. Astereognosis without marked elementary sensory loss seems to result from injury higher up in the superior parietal lobule although difficulty in the recognition of form with gross sensory loss occurs from lesions anywhere in the somesthetic cortex.

When lesions of the left hemisphere occur in right-handed persons anywhere in a broad band stretching backward from the posterior part of the middle and inferior frontal convolutions as far as the angular gyrus and covering the lower parts of the anterior and posterior central gyri, the supramarginal gyrus, the angular gyrus, the superior temporal gyrus, and, in the depths of the lateral fissure, the island, troubles of the anarthria-aphasia-apraxia series occur (331). Analysis of the war-wounds seems to indicate the distribution shown in Figure 28; analysis of vascular cases is in general agreement (359).

In an area (A) which covers the posterior extremity of the middle and inferior frontal convolutions with the lower end of the anterior central gyrus, a wound causes an anarthria, associated often with alexia, agraphia, and contralateral facial weakness. The zone (B) of the supramarginal gyrus gives rise to a global aphasia with loss of vocabulary

prominent; there is usually associated with it a brachial monoplegia and hemianesthesia; ideomotor apraxia is the rule with predominance in the right hand; there is no hemianopia. With injury of the angular gyrus (C) occurs a hemianopia, complete or quadrantal; there is no hemiplegia and no hemianesthesia; there is no anarthria but an aphasia in which alexia predominates. Injury to the superior and middle temporal convolutions (D) causes a typical aphasia in which auditory verbal agnosia predominates, with paraphasia, jargonaphasia, perseveration, and loss of vocabulary; there is a hemianopia, often of inferior quadrantic type, but no hemiplegia or hemianesthesia. There is also an intermediate zone (E) over the island where wounds, especially if they be deep, lead to a profound aphasia and anarthria with a severe hemiplegia.

From a study of the data which we have just outlined it follows that the results of electrical stimulation of the cortex, the results of occlusion of bloodvessels, and the results of direct traumatic destruction of the cortex and its subjacent white matter are roughly concordant. They also agree fairly well with what we know of the *fiber-tract connections* of the various cortical areas.

The transverse temporal gyri, the posterior central convolution, and the calcarine region have a similar cortical structure which we have distinguished as the koniocortex. Into the transverse temporal gyri stream centripetal fibers radiating from the inferior colliculi and internal geniculate bodies which are known to be relay-stations for the central auditory pathways. Electrical stimulation in the neighborhood of these gyri causes auditory hallucinations, and bilateral destruction of them causes deafness. The conclusion that the fibers of this radiation carry incoming auditory impulses is consistent with all the evidence. The pathway of the visual impulses from the retina to the striate cortex of the occipital lobe is even more certainly known in great detail. The somesthetic pathway through the thalamus to the posterior central region is also definitely known (Fig. 29).

A correlation of the cytoarchitectural studies of the cortex with stimulation-experiments and with the results of injuries to the brain makes it evident that voluntary motion is initiated by impulses, from the large Betz-cells of the anterior central region, which pass centrifugally over the cerebrospinal or pyramidal pathways (85). The areas from which complex turning movements of the head, eyes, and trunk to the opposite side can be elicited by electrical stimulation differ somewhat in structure but a study of the deeper relations of these areas shows that

in their neighborhood arise the cerebropontine tracts, if we accept the origin of the frontopontine tract in man to be the same as in lower vertebrates, for example in the opossum (326). Its exact origin in man is still in dispute among anatomists; by some it is supposed to arise farther forward in the frontal lobe. There is a region in the inferior frontal gyrus where the pyramidal cells of the fifth layer are especially abundant (field FDI of Economo and Koskinas); its significance is not clear. There is also an efferent pathway from field OA of the occipital cortex. These efferent pathways are shown in Figure 29.

The anatomical correlates, therefore, of such relatively simple functions as sensation and voluntary motion are somewhat familiar to us. We know also that the central mechanism of the more complicated function of language is usually clustered closely around the lateral fissure, but when we attempt to discuss a higher mental function, such as intelligence, we are greatly hampered by lack of consistent data. Yet certain areas of the brain are known, injury to which is peculiarly liable to disturb intelligence. One of these is the left occipitotemporal region. Another is the interior part of the frontal lobe, although in this case the disturbance of character is predominant and I should be less willing to indicate the exact area involved. It is significant that these parts are just the ones in the human brain which are most developed beyond those present in the higher apes.

Of course one has still to explain why, for example, injuries to the tight supramarginal gyrus, which is as well developed as the left, should not cause any defect. That is a complicated problem which I will not discuss. Some of the defects which are produced by injuries to the brain subsequently disappear; possibly other areas are able to take over the function of the injured part. But the student should not be misled by reports of removal of the frontal lobe, or of other parts of the brain, without resultant symptoms. Such reports mean only that the observer was not keen enough to detect the loss (241). Should the student try such a mutilation of the brain he would find not only that there are symptoms but that they are often discouragingly persistent.

All of which goes to show that the different parts of the human cerebrum are not equipotential. The brain cannot be insured with impunity and one must enter it with full knowledge of what the consequences may be. The symptoms which may be expected from injuries to various areas of the left cerebral cortex we may summarize in two diagrams (Fig. 30). We have not discussed the cerebellum;

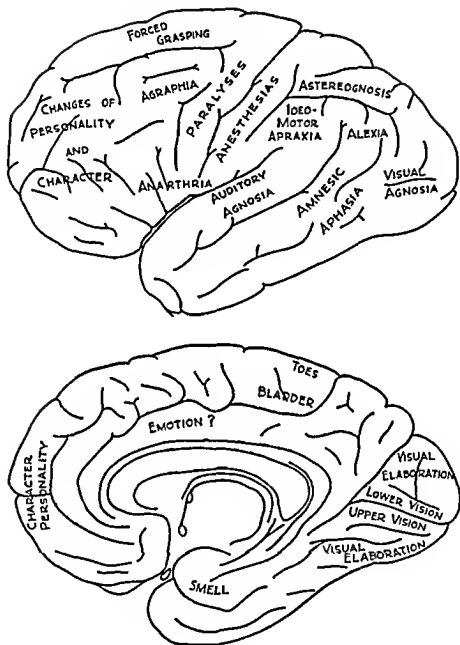


FIG. 30. Scheme of the left cerebral hemisphere—above, the lateral surface indicating the various symptoms resulting from injury to certain zones; below, the median surface showing functions disturbed by injuries in various regions.

occasion will be found to do so later and also to examine briefly the deeper gray masses of the cerebrum. I merely wanted to impress upon you that *in the human brain the parts are not equipotential and that even the defect of intelligence does not, as is sometimes stated (310), depend only upon the quantity of cerebral tissue removed or destroyed.*

CHAPTER 4

THE ACOUSTIC NEURINOMA

SYNDROME OF THE CEREBELLOPONTINE ANGLE

As an example of how each intracranial tumor should be studied it would be difficult to find one more suitable than the acoustic neurinoma. With it we will begin our detailed analysis of the symptomatology, diagnosis, and treatment of the various types of intracranial tumors. The acoustic neurinoma was perhaps the first to be treated in this way in a dissertation by Folke Henschen published in 1910. I will show you some patients with fairly typical symptoms so as to bring the matter graphically before you.

This young workman (CASE 1), twenty years of age, appears somewhat thin and asthenic, but seems quite well as he sits on his chair before us except that the left side of his face droops and the left eyeball is rotated slightly inward. The lack of parallelism of the two eyes is more evident when the patient is asked to look to his left side without turning his head; the left eye does not move outward beyond the midline (Fig. 31). This means, of course, a paralysis of the external rectus muscle, which is innervated by the sixth cranial nerve. You see also that the nasolabial fold on the left side of the face is not so evident as on the right side, the left upper lip lags, and the left eye does not close completely. These are indications of weakness of the facial muscles of the left side of the face, innervated by the seventh or facial nerve. The left acoustic nerve is also affected. If I close the right external acoustic meatus with my finger and speak to him in an ordinary tone of voice he does not respond. When I ask him to open his mouth widely the lower jaw deviates to the left, which means that the pterygoid muscles on the left side are weak; they pull the condyles of the jaw forward, the left one being weak the jaw is dislocated to the weak side. The left masseter muscle is also weak as we can prove by asking him to clench his teeth. Palpation of the masseter muscles shows that the left one contracts much more feebly. These muscles are both innervated by the trigeminal nerve, which supplies also cutaneous sensation to the face. Although it is difficult to demonstrate any loss of sensation over the skin of this boy's

face, the cornea on the left side is clearly not normally sensitive because when cotton-wool is drawn across it he does not wink or flinch, whereas similar stimulation of the right cornea causes withdrawal, an expression of pain, and profuse flow of tears.

The fifth, sixth, seventh, and eighth cranial nerves are, therefore, affected on the left side. Nor is this all. When he is asked to open his mouth widely and I touch the posterior wall of the pharynx on the right side he gags, but when I touch the left side he makes no

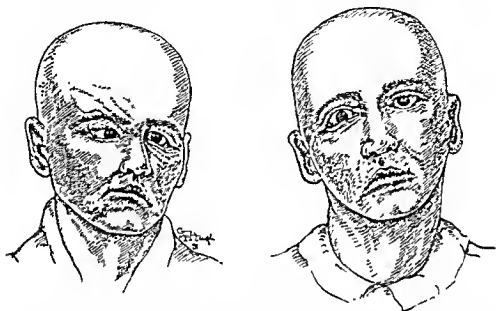


FIG. 31. Patients with acoustic tumor. At the left, CASE I with left facial paresis and paralysis of the left sixth nerve (patient looking to the left); at the right, CASE II with a right facial paresis, weakness of both sixth nerves and the head tilted to the right.

objection. If he tries now to say *Ah* you may see that the palate moves upward on the right side but that the left side lags behind. Sensation of the pharyngeal wall is carried through the glossopharyngeal nerve, but complete transection of this nerve causes no paralysis (24). Weakness of the palatal musculature appears only when the tenth nerve is affected. The sternomastoid muscles are both of equal power and the tongue is protruded in the midline without tremor or atrophy; the eleventh and twelfth cranial nerves are, therefore, normal.

There is, then, paresis of the cranial nerves on the left side from the fifth to the tenth, inclusive. These nerves all emerge from the brainstem in the cerebellar fossa in the neighborhood of the pons and

cerebellar peduncles. It is easy to show that the cerebellar apparatus on the left side is also affected. When he puts his left hand to his nose the unsteadiness of the movement is very pronounced and when he tries to walk his gait is reeling, with a very definite deviation and tendency to fall to the left side.

This combination of unilateral involvement of the cerebellum with multiple pareses of the homolateral cranial nerves of the cerebellar fossa is known as the SYNDROME OF THE CEREBELLOPONTINE ANGLE. The story of how it was produced in this boy is as follows: He had always considered himself well until about a year ago, when he began to stagger in walking. This trouble annoyed him at his work so he consulted a physician who made a lumbar puncture and, although the cerebrospinal fluid was normal, he was treated with intravenous injections of neoarsphenamine for five months. During this time there seems to have been no other complaints and no other symptoms could be elicited except slight difficulty in hearing with the left ear. This slight deafness had been present for a long time, it is not known how long, but when he went to work for the telephone company more than two years previously he already had to listen to the telephone with his right ear. After his injections he had moderate headache but only vomited once following his lumbar puncture. He continued fairly well until a month before admission although he had become completely deaf in the left ear and his speech was indistinct. Then another lumbar puncture was made, after which he was much worse; the left arm and leg became weak; walking became almost impossible, and there developed some blurring of vision. A neurologist was called in consultation who sent him to this clinic.

When he was admitted to the hospital he could walk only with assistance; when left to himself he staggered and fell to the left and backward. He lay usually in bed with a rather blank expression on his face and when questioned answered slowly after a long pause, with a thick and indistinct articulation. There was a convergent squint to the eyes due to weakness of the left external rectus muscle. When he was asked to look to the right and then to the left there developed a nystagmus which was less evident and more rapid when he looked to the right. The left corneal reflex was weaker than the right. The retinal veins were congested and the optic disc was swollen and elevated 2.5 diopters on the right side and 4.0 diopters on the left side. The left side of the mouth drooped and he could not close the left

eye well. He could not taste well on the left half of the tongue. He was completely deaf in the left ear and irrigation of this ear with cold water provoked no nystagmus and no dizziness. The left side of the palate lagged when voluntarily innervated. He choked when swallowing and his voice was hoarse. There was a very marked incoördination of the left arm and leg; movements of the right arm and leg were fairly steady. He could not walk without assistance, but reeled to the left and often fell backward. There was no exaggeration of the tendon-reflexes on either side and no sensory loss over the body and extremities. A roentgen examination of the head revealed no abnormality of the skull.

He had at that time, therefore, a syndrome of the cerebellopontine angle much more marked than at present and symptoms of increased intracranial pressure besides. Moreover, deafness of the left ear seems to have been the earliest symptom. A diagnosis of acoustic neurinoma was made, with some hesitation because of his age, and a suboccipital craniectomy was performed under local anesthesia. The smooth surface of a reddish-yellow tumor was found in the left cerebellopontine angle. The ninth, tenth, and eleventh cranial nerves could be seen stretched around its inferior extremity. There was a large cyst formed by the thickened arachnoidal membrane over the tumor. This was emptied of its yellowish fluid. An incision was then made through the capsule of the growth and its contents removed with a soft metal spoon. No attempt was made to remove the capsule. It is now seventeen days after the operation. His incoördination is much improved. He walks without assistance, but is still unsteady and reels to the left. His speech is more distinct and he no longer chokes when swallowing. He has no headaches. The swelling of the optic discs has subsided. The facial weakness is, however, more apparent.

This is a fairly typical clinical record of an acoustic neurinoma, except for the age of the patient. Analysis of a large number of cases shows that the average age of onset of symptoms is around thirty-five years (Fig. 32).

—The other patient (CASE II) which I have to show you is a young woman of thirty-six who has been deaf in her right ear as long as she can remember, but otherwise quite well until seventeen months before admission. At this time she began to have some defect in speech. Shortly afterward she noticed that the right hand was uncertain in its movements and she began at times to stagger to the right in walk-

ing. At about the same epoch, for a period of two or three weeks, she had severe frontal headache; since then the headache only occasionally recurred. About two months before admission the right side of her face began to feel numb. Lately she saw double and the vision of the right eye was blurred.

When admitted she was in good general health. There was no tenderness or stiffness of the neck but the head was held tilted to the right (Fig. 31). On looking to the left there was a very rapid fine nystagmus; on looking to the right the nystagmus was much coarser

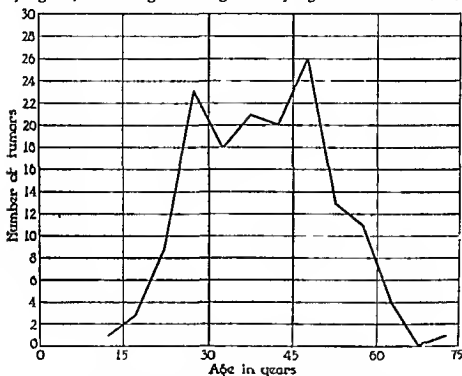


FIG. 32. Graph of age-distribution of acoustic neurinomas.

and slower. The quick component of the nystagmus was always outward. The optic discs were swollen 3-4 diopters; the visual fields were normal. The right corneal reflex was absent. There was a weakness of both sixth nerves. The entire right side of the face was hypoesthetic and there was a weakness of the entire right facial musculature. The right side of the palate lagged both on voluntary and reflex stimulation. The right ear was deaf and there was no response of the right labyrinth to caloric tests. The hearing was also diminished in the left

ear in which she had a chronic suppurative otitis media. The left labyrinth responded fairly well to caloric tests. The speech was dysarthric. There was slight tremor of the right hand and slight but definite incoördination of the right arm and leg. The gait was unsteady with a tendency to deviate to the right. The tendon-reflexes on the right side were feeble. Roentgenogram of the head showed the right internal acoustic meatus to be dilated (Fig. 33).

This patient also had pareses of the fifth, sixth, seventh, eighth, ninth, and tenth nerves with symptoms of cerebellar involvement. The

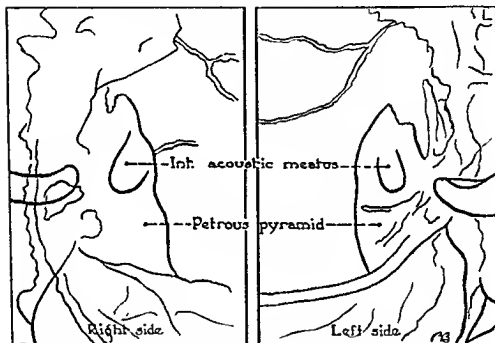


FIG. 33. Schemes from the roentgenograms of CASE II. Compare Plate I.

intracranial tension was obviously high and the deafness of the right ear preceded the other symptoms by many years. A diagnosis of right acoustic neurinoma was made.

Suboccipital exploration disclosed a smooth tumor high up in the right cerebellopontine angle. The lobulus biverter and outer half of the lobulus gracilis were removed from the right cerebellar hemisphere giving an excellent approach to the tumor. The capsule was incised and the interior of the growth removed until the capsule could be collapsed. Bleeding was carefully checked and the wound closed. She recovered promptly. The swelling of the optic discs subsided rapidly.

It is now twenty-seven days after operation. There is still the same nystagmus as on admission. The right facial weakness is less. The right corneal reflex is present but sluggish and there is some slight hyposthesia of the ophthalmic division of the right trigeminal nerve. Very little dysarthria remains. There is a very slight incoordination of the right arm but a very marked incoordination of the right leg and some also of the left leg. She can walk alone but her gait is quite unsteady. The head is held tilted to the right and the entire body is curved with concavity to the right. We see, therefore, that although she is much more comfortable, some of the cerebellar symptoms are more marked than before, and these doubtless result from removal of the lobulus biventer.

In these cases the tumors were so large that it would be impossible at operation, perhaps even at necropsy, to be sure of the exact origin. But examination of a number of very small tumors of this sort has demonstrated the interesting fact that they arise usually, perhaps always, within the internal auditory canal and from the vestibular division of the eighth nerve. If we turn for a moment to the normal STRUCTURE AND DEVELOPMENT OF THE ACOUSTIC NERVE we may gain some clue to the reason (443).

The eighth nerve first becomes visible in the embryo as a group of cells, lying medial and ventral to the auditory vesicle, known as the acoustico-facial ganglion. The facial portion is early distinguishable by its pale staining and the larger size of its cells. The remainder of the triangular mass is undifferentiated but eventually divides into the dorsolateral vestibular ganglion and the dorsomedial cochlear ganglion. The cells of these ganglionic groups differentiate in two directions; part of them become bipolar nervous cells, and others become the subcapsular satellites of the nervous cells and the neurilemmal cells of the sheaths of their fibers. The vestibular ganglion-cells are the first to put out fibers toward the auditory vesicle, followed shortly by the cochlear. From the other extremities of the bipolar cells, fibers enter the brainstem to form the intracranial portions of the vestibular and cochlear divisions of the acoustic nerve. These fibers are accompanied by neurilemmal cells from the same source but the nervous fibers outgrow them. Also from the brainstem neuroglial cells migrate outward along the ingrowing fibers and the two types of covering-cells meet at a variable distance from the brainstem.

The acoustic nerve is about 17-19 mm. in length in an adult male.

Microscopically it is clearly divided into two parts, a proximal and a distal part, of quite different structure. The proximal part, for an average distance of 10-13 mm. from the brainstem, is composed, in addition to the nervous fibers, of neuroglia. The distal portion has, on the contrary, the structure of a peripheral nerve; perineurium, epineurium and endoneurium, and neurilemmal sheaths are clearly discernible. The point of junction of the two portions lies about the level of the porus acusticus internus.

The junction of neuroglia and perineurium is usually located somewhat more distally on the vestibular nerve, which also contains much more connective tissue. Its perineurium and epineurium are especially distinct. Whereas in the cochlear ganglion the subcapsular cells are regularly arranged and placed beneath the capsules of the ganglion-cells, in the vestibular ganglion there is an excessive number of irregularly situated cells resembling subcapsular or neurilemmal cells lying in a disorderly fashion between the ganglion-cells.

The origin of these neurinomas is evident from their microscopical structure. They must arise from the distal part of the nerve because the neoplastic cells resemble the neurilemma. Actually the earliest tumors of this type have been found in the porus acusticus internus as expected from this theory. It is not so clear why the tumor should arise from the vestibular division except possibly that there seems a normal tendency in its ganglion to overproduction of neurilemmal cells.

THE GROSS APPEARANCE OF THE TUMOR, as it is usually seen at operation or necropsy, is characteristic (Fig. 34). After it has reached a size sufficient to kill the patient or cause him to seek relief at the hands of the surgeon, it varies in size from 4-7 cm. in diameter. It lies in the angle between the petrous pyramid, the tentorium cerebelli, the cerebellum, and the brainstem. It is closely applied to the petrous pyramid and base of the skull, to the irregularities of which it usually conforms, but the surface which compresses the cerebellum is smooth or only grossly nodular. The color is pinkish-gray with often yellowish areas. The yellowish areas are much softer; the grayish areas quite firm. Over the surface of the growth run irregularly many branches of the basilar artery destined to supply the cerebellum. They are also densely adherent. Similarly large veins are scattered about, apparently with no definite plan. The tumor compresses the sigmoid sinus and may even extend through the jugular foramen. The whole group is surrounded by a capsule of arachnoidal membrane, clearly visible at

operation, but difficult to demonstrate at necropsy. This capsule contains a variable quantity of fluid, often sufficient to form a veritable cyst over the posterior surface of the growth. The cyst is obviously formed by accumulation of cerebrospinal fluid in the lateral cistern of the subarachnoid space.

When the subarachnoid membrane is removed the relations of

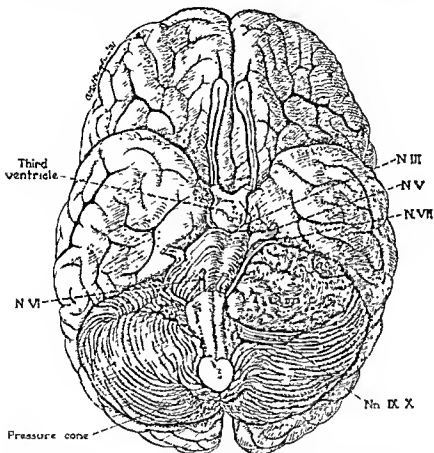


FIG. 34 Base of the brain with an acoustic tumor in place. Note the pressure-cone, dilated infundibulum and stretching of the fifth, seventh, ninth, and tenth nerves.

the tumor to the cranium may be studied. If the tumor is small the acoustic nerve may be found entering the medial surface of the tumor; if the tumor is large it may be impossible to identify it (347). The peripheral part of the nerve is never visible. The facial nerve is stretched tightly over the anterior extremity of the tumor and flattened

into a narrow ribbon which may be discoverable only on microscopical examination. It is elongated at times to as much as 5 cm. The fifth nerve is also compressed and elongated by the anterior pole of the growth. The sixth nerve, however, usually lies free. Around the inferior extremity the ninth, tenth, and eleventh nerves are similarly elongated and compressed. It is possible to dissect free the fifth, ninth, tenth, and eleventh nerves, but often the seventh is too firmly adherent. The cerebellum and brainstem are pushed aside and deeply indented; the latter suffers most. The cerebellum is also thrust downward through the foramen magnum by the tension above; the imprint of the latter is clearly visible and the tonsils are herniated downward to form what is known as a "pressure-cone." The tumor almost invariably extends deeply into the internal acoustic meatus. This extension is broken off when the tumor is removed. The internal acoustic meatus is often enlarged and the petrous pyramid extensively eroded.

There is almost always a certain degree of internal hydrocephalus which is visible on the under surface of the brain as a marked distension of the infundibulum. The sella turcica is correspondingly eroded, the dorsum and clinoid processes being atrophic and shatpened. There may be multiple small herniations of the cerebrum through the openings of the arachnoidal granulations.

The MICROSCOPICAL STRUCTURE of the tumor is quite characteristic also (Fig. 35). It is made up of two types of tissue. There is in the first place a reticulated tissue in which the boundaries between the cells are not very distinct. Here the cytoplasm seems to form an interlacing network of broad bands between which are edematous spaces and numerous rounded cells full of lipoidal granules. The cytoplasm has in most instances undergone a hyaline transformation. Small darkly-stained nuclei lie here and there in the cytoplasm and scattered bands of reticulin traverse the loose tissue in various directions. These areas are obviously undergoing an extensive degenerative change. The denser tissue is composed of interlacing streams of very elongated narrow bipolar cells. Their cytoplasm is scanty and extends from each extremity as a delicate strand. The nuclei are very elongated and shaped somewhat like sausages; when cut in cross-section they appear small and round. Parallel to the long axes of the nuclei is an unbelievable number of delicate strands of reticulin (376). Collagen is present only around the bloodvessels except near areas of degeneration. Elastin is almost never found and fibroglia rarely. Mitoses are rarely seen.

There is often a characteristic tendency for the nuclei to lie parallel to each other to form a sort of palisade. This arrangement is found in some other tumors, such as myomas of the uterus, but rarely in any other intracranial tumor. The *myriads* of delicate fibers of reticulin and the palisading of the nuclei serve to identify an acoustic tumor.

The SYMPTOMS OF ACOUSTIC TUMORS are fairly consistent. When one remembers that all of the early tumors heretofore described developed from the vestibular division of the acoustic nerve, it is strange that the vestibular symptoms do not often figure prominently in the

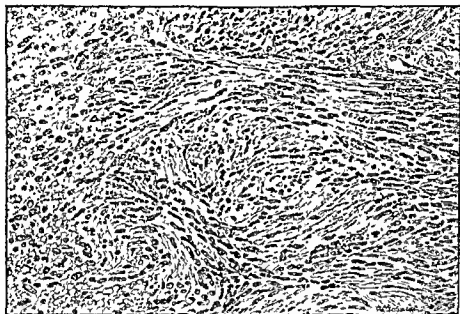


FIG. 35 Microscopical drawing of an acoustic neurinoma. Note the streams of cells and the tendency toward palisading of the nuclei.

early history of these patients. Yet in most instances symptoms are first noted from the cochlear division. But a few cases are recorded in which the clinical history began with attacks of vertigo and dizziness so severe as seriously to inconvenience the patient. Vertigo occurs in two forms; in one there is a definite sense of movement of self or of surrounding objects, in the other it is an indefinite sensation generally described as a "giddy feeling." The sense of displacement of external objects is from the side of the lesion to the opposite side, whereas the subjective rotation of self is always from the healthy side

toward the side of the lesion. A sensation of unsteadiness and instability of gait is frequently present later in the course of the disease but at this time it is difficult to distinguish the rôle played by the vestibule from that of the cerebellum.

In the vast majority of cases the inaugural symptoms are auditory. Tinnitus or deafness may precede other symptoms by a few months or as much as a decade. It is always possible that in doubtful cases a preëxisting deafness was overlooked. Experience shows, for example, that an increasing deafness of the right ear is unperceived much longer than a deafness of similar degree of the left ear, because the left ear is used for listening to the telephone. Tinnitus usually precedes the deafness. The noises heard are variously likened to rushing, roaring, buzzing, swishing, or ringing sounds. They are usually referred to the deaf ear, but may be referred to the opposite ear, and occasionally are bilateral. The defect in hearing usually progresses steadily from the appearance of tinnitus to practical or complete deafness, but occasionally a sudden deafness seems to appear relatively late in the course of the disease. Rarely there is no deafness on the side of the tumor.

We have seen that the fifth, seventh, ninth, tenth, and eleventh nerves are elongated and distorted by the tumor. As might be expected symptoms referable to these nerves appear later and are more often absent than the auditory symptoms. Symptoms of irritation of the facial nerve are not uncommon and consist of spasms or twitchings which may be more or less constant or come on in attacks so that a mistaken diagnosis of focal epilepsy is made. Rarely a spasmodic tic may be the first symptom of an acoustic tumor. The slight facial weakness frequently present is usually overlooked by the patient. Probably after the eighth, the fifth nerve is the one from whose involvement the patient is most apt to notice symptoms. Paresthesias are variously described, such as numbness, tingling or burning sensations in the face, and the mucous membranes may also rarely be involved. Actual pain is uncommon (367) and when present usually slight and transitory. Rarely paroxysms of pain occur early which may lead to an erroneous diagnosis of major trigeminal neuralgia. A subjective disturbance of taste is frequently noted and may be explained by involvement of the fifth, seventh, and ninth nerves, all of which are impaired by the growth.

Symptoms of involvement of the ninth, tenth, and eleventh nerves appear late. Prominent among them are difficulty of swallowing and

of articulation. The patient becomes conscious that the act of swallowing requires more effort and that food is apt to return into the nasal passages or into the larynx and cause coughing and sneezing. The speech also becomes thick, slurred, and indistinct. Diplopia is a frequent symptom although it has been shown that the eye-muscle nerves are not directly affected by the growth. The sixth nerve is most frequently involved, probably compressed by some branch of the basilar artery.

Preceding the involvement of the cranial nerves, concomitant with it, or more rarely much later, appear symptoms of derangement of the cerebellum. The patient may notice a tendency to drop things from one hand. Usually, however, the involvement of the upper extremity is slight. The lower extremity is much more affected and the gait becomes unsteady and reeling and there is a tendency to deviate or fall to the side of the tumor. The incoördination may become so great that the patient is completely bedridden.

Often early in the course of his illness the patient is conscious of a stiffness of the muscles of the neck on one side and this discomfort may progress to actual pain which radiates to the frontal region. Later there is generalized headache, vomiting, and failing vision from general intracranial hypertension.

The OBJECTIVE SIGNS of course vary with the progress of the disease, but when the patient presents himself for examination in a moderately advanced condition he is usually dull and apathetic from the pressure of an internal hydrocephalus. He walks with a reeling gait, with a definite tendency to deviate and fall to one side. The head is held tilted to the affected side, probably from unilateral vestibular defect. There is a strabismus from involvement of the sixth nerve. The suboccipital region is tender to pressure, especially on the deaf side, and the patient resists any attempt to flex the chin on the chest from fear of a resultant headache. When asked to look first to one side and then the other nystagmoid movements of the eyes are provoked, with the quick component outward. The nystagmus is slower and more evident on looking to the side of the lesion. The optic discs are choked and visual acuity may be reduced. There is a hypoaesthesia of the fifth nerve, usually evident only by the absence of the corneal reflex, but a generalized hypoaesthesia to all forms of sensation may be found. Atrophy of the muscles of mastication is uncommon but the jaw may deviate to the affected side. One eye fails to rotate out-

ward. There is a weakness of the face on one side which is often so slight that you see only on one side of the mouth an inconspicuous drooping which disappears on voluntary movement. The ear on the affected side is almost or totally deaf; sometimes an island is found where certain tones are retained. Vestibular tests on the affected side give no response and there is also no response from the vertical canals on the opposite side (473). The palatal reflex on one side is absent and the soft palate on that side lags on voluntary movement. The tongue almost invariably protrudes in the midline. All of the signs of involvement of the cranial nerves are usually on the deaf side but some of the nerves may be involved bilaterally or contralaterally. Such contralateral signs are probably the result of the extraordinary distortion of the brainstem. The fifth and eighth nerves are those most likely to be involved on the opposite side. Except for the symptoms of the acoustic nerve the disturbances of the other nerves fluctuate greatly in intensity. This fluctuation is probably related to the arachnoidal cyst which surrounds the tumor. The involvement of the cerebellum and its peduncles is evidenced by the asynergia, hypotonicity, and hypermetria of the arm and leg on the deaf side. The reeling gait and deviation to one side when walking are other evidences of the same disturbance.

Due to the pressure of the tumor on the bulb the sensory or motor tracts are compressed in the later stages of the disease giving rise to a sensation of numbness in the arms and legs and exaggeration of the reflexes. Usually these symptoms are bilateral but may be contralateral and the numbness is often homolateral. When the intracranial tension is very high, of course, coma may occur with respiratory difficulties. There occur also attacks of so-called "cerebellar" seizures during which the neck is retracted, headache is intense, the pulse-rate is slow, respiration is embarrassed, and the patient may become unconscious.

From the study of a long series of cases (122) it has been found that the symptoms usually occur in the following order: (1) auditory and labyrinthine symptoms; (2) suboccipital discomfort; (3) incoördination and staggering gait; (4) involvement of adjacent nerves; (5) headache, vomiting, and choked discs; (6) dysarthria, dysphagia, cerebellar seizures, and respiratory difficulties. This order may be interpreted from the pathological anatomy to mean that the tumor arises from the eighth nerve and presses first against the cerebellar peduncles, later involving the adjacent nerves. The circulation of the cerebrospinal

fluid is finally impeded, causing an internal hydrocephalus and increased intracranial tension. With increasing size of the tumor the ninth and tenth nerves are involved, and finally the compression of the brainstem becomes extreme, causing respiratory difficulty and temporary periods of bulbar anemia.

The DIAGNOSIS OF AN ACOUSTIC TUMOR is difficult in the early stages of its growth (203). It must be differentiated from all the multifarious affections of the internal ear causing deafness or tinnitus and vertigo. The diagnosis will, of course, be much more difficult in those rare cases of bilateral tumor. Careful examination of the external and middle ears will clear up many doubtful cases, and a history of otitis media will give a clue to cases of arachnoiditis in the homolateral angle. It is in chronic or subacute affections of the internal ear unassociated with suppuration that most difficulty will arise. Such conditions, however, are usually bilateral and it is only the rare cases in which the disease predominates markedly on one side that are confusing. The most frequent conditions to be differentiated are otosclerosis, syphilitic labyrinthitis, toxic neuritis, senile or arteriosclerotic deafness, and hemorrhage into the labyrinth.

Otosclerosis is a disease more frequent in females. It begins usually in young adult age. It is usually bilateral. In 50 percent of the cases there is a definite hereditary taint. Examination shows that conduction by bone is lengthened, and longer than conduction by air; the lower limit of perception of sound is raised. Vertigo is a minor symptom of otosclerosis. Syphilis of the internal ear is characterized by suddenness of onset of tinnitus and vertigo followed by rapid progression of deafness. There is marked diminution of perception of sound through the cranial bones and conduction by air is definitely longer than conduction by bone. It is usually a bilateral affection. Senile or arteriosclerotic deafness is usually bilateral and not accompanied by giddiness; the age and general condition of the patient indicate the nature of the affection. ✓ Labyrinthitis from leukemia, nephritis or drugs, may be suspected from the history and general examination and, in these conditions, one does not find complete deafness or total loss of vestibular reactions.

The positive diagnosis of an acoustic neurinoma is based largely upon the characteristic progression of symptoms. The tumor must be differentiated from other types of tumor developing in the same region and giving rise to the syndrome of the cerebellopontine angle. The characteristics of the syndrome of the cerebellopontine angle are evident

from the name and consist of symptoms of involvement of the fifth, seventh, eighth, ninth, and tenth nerves combined with symptoms of homolateral involvement of the cerebellum. It is obvious that any expanding lesion in the angle between the petrous pyramid, tentorium, cerebellum, and pons may cause such a combination of symptoms. But experience has shown that *unless the symptoms appear in characteristic order an acoustic tumor cannot be diagnosed with certainty.*

The lesions most frequently confused with acoustic tumor are the following:

1. Glioma of the pons (277). A glioma developing within the brainstem in the neighborhood of the point of entrance of the eighth nerve may give rise to a clinical disturbance beginning with tinnitus or deafness and vertigo, followed by cerebellar disturbances and involvement of the other nerves in the angle so that a differential diagnosis is difficult. Usually, however, such tumors occur in children, bilateral involvement is more frequent, pyramidal and sensory disturbances are more evident, and symptoms from intracranial hypertension are late to develop or absent. Optic neuritis is usually absent; headaches are less intense. Pareses of conjugate lateral movements of the eyes are frequent.

2. Meningiomas of the angle. Such tumors may give a complete syndrome which is only to be differentiated by the fact that acoustic symptoms were late to develop. Rarely such a tumor develops in the internal acoustic meatus; the differentiation then becomes impossible.

3. Perhaps the most frequent source of error is to be sought in the localized arachnoiditis of the lateral cistern. Especially is this the case when the corresponding ear is defective from an old infection which may have provoked the chronic arachnoidal thickening. The symptoms of chronic serous arachnoiditis are notoriously fluctuant but so are those of acoustic neurinomas and probably for the same reason. We have noted how often an acoustic tumor is surrounded by an arachnoidal cyst. In either case the symptoms may be relieved by lumbar puncture. Even at operation the confusion does not cease for very often the surgeon has evacuated the cystic accumulation of fluid around a tumor of the angle and, failing to dislodge the tumor, has recorded the case as one of arachnoiditis, only to have the growth demonstrated by the pathologist at necropsy.

4. Intracerebellar tumors (457). The symptoms of increased intracranial tension appear early and palsies of the cranial nerves are

usually late and slight. The trigeminal nerve is rarely involved. Weakness of the palate or vocal cords, difficulty of swallowing, and disturbances of phonation are absent. The hands are less ataxic. Crossed hemiparesis is absent.

The surgeon would be delighted to have acoustic tumors diagnosed in the early stages of their evolution when only the eighth nerve is involved by a small tumor. Such a diagnosis would be based on unilateral tinnitus, deafness, and vestibular symptoms such as vertigo. Tinnitus and vertigo, however, are common symptoms and apparently those which accompany the development of an acoustic tumor differ in no wise from other cases in which there is no tumor present. It is unlikely, therefore, that a diagnosis will often be made until trigeminal paresthesia, facial spasm, suboccipital discomfort, unsteadiness of gait, or other symptoms point to an expanding lesion.

We have noted that acoustic tumors apparently arise within the internal acoustic canal and certainly there is nearly always an extension of the tumor into the canal which is widely dilated. It would seem to be easy to demonstrate this dilatation with the roentgen rays. Practically, however, this demonstration is very difficult and when made rarely aids in the diagnosis because by that time the other symptoms make the diagnosis obvious. There may also be an extensive erosion of the petrous pyramid visible in the roentgenogram (470), rather characteristic of acoustic tumors. Finally another factor may be mentioned which will aid in the diagnosis. It has long been known that although acoustic tumors usually are solitary, *they may be bilateral and furthermore associated with a more widespread disturbance known as generalized neurofibromatosis* (of von Recklinghausen) (466). In these cases the pigmented areas and peripheral tumors will point the way to a correct interpretation of the intracranial condition. The intracranial situation is sometimes complicated also by the occurrence in these cases of multiple meningeal tumors. Rarely an acoustic tumor seems to be hereditary (209).

The only known TREATMENT for an acoustic tumor is to remove it by surgical operation. Obviously also the earlier the diagnosis is established, the smaller will be the tumor and the easier will be its removal. Although any case of unilateral tinnitus or increasing unilateral deafness in an adult, with no history of suppuration in the middle ear, should be suspected of being caused by an acoustic tumor, especially if the patient has signs of a generalized neurofibromatosis, it probably will be

long before either otologist or neurologist will be willing to advise operation in the absence of confirmatory evidence. But such a patient should be watched closely for the symptoms which habitually appear next in the presence of tumor, namely, paresthesias in the trigeminal area with absence of the corneal reflex, pain and stiffness in the neck on the same side, or more rarely spasm and twitching of the facial muscles. Even at this stage operation is rarely undertaken.

By the time the diagnosis is established and the patient is willing to submit to operation, the tumor is already voluminous and involved in a tangle of nerves and bloodvessels as we have already described. Moreover, direct access to the tumor is barred by the middle and inner ears, the mastoid cells and the sigmoid sinus. Attempts to reach it by a direct approach have been uniformly unsuccessful and generally abandoned for a more indirect approach through the suboccipital region below and behind the sigmoid sinus. The latter approach is cramped for room so that attempts completely to enucleate the tumor were long unsuccessful because the surrounding structures could not adequately be brought into view. If the patient did not die immediately from hemorrhage he was left with a paralysis of the seventh, sometimes also the fifth, ninth, tenth, and eleventh nerves. Under these circumstances the established mode of operation came to be to split the capsule of the tumor and remove the interior by means of a soft spoon (122). The fatty degeneration which the tumor undergoes made this procedure easier by softening its consistency and reducing the bleeding. If enough of the tumor was extirpated the capsule collapsed and removed the pressure on neighboring structures. The patient was thus relieved of his symptoms for a period of years with a minimum of injury to the nerves and a minimum risk of death from hemorrhage. By operating in that way, the mortality was not greater than 15 percent but permanent cures were not effected. The intracapsular operation was unsatisfactory in the long run and a new operative approach which permitted more complete removals with equal safety was sought. With minor variations, the tumor is now almost universally attacked through a unilateral suboccipital approach and complete extirpation is often accomplished (278, 364).

CHAPTER 5

HYPOPHYSIAL ADENOMAS

ACROMEGALIC SYNDROME

HYPOPITUITARY SYNDROME

In 1886 Pierre Marie described a new clinical syndrome and gave it the name of acromegaly. When in the following year Minkowski suggested that the disease was caused by derangement of the hypophysis cerebri, attention was focused upon this obscure structure. It was found that acromegaly was almost always associated with a tumor of the hypophysis. But an apparently quite similar tumor occurs with no signs of acromegaly and clinicians were long puzzled to explain the difference in symptoms. The two contrasting conditions are well demonstrated by the patients which I will now present.

The first patient (CASE III), with a typical ACROMEGALIC SYNDROME as described by Marie, is a married woman of forty-eight years. Her menses were always scanty and painful but she considered herself well until seventeen years ago when she began to suffer from headaches back of her eyes, which were somewhat relieved by pressure in the temporal regions. Even before the headaches began someone remarked that her hands were big but after this time they seemed to increase rapidly in size, also her feet. The features of her face coarsened. Soon her teeth were so widely spaced that food collected between them. Her tongue also became thick and she was apt to bite it when chewing her food. These changes came on gradually and have continued to progress. She was married seventeen years ago and nine years later had to have her wedding-ring sawed off. Some three years after the onset of these symptoms of overgrowth she began to sweat profusely. Now she complains chiefly of this sweating which has a disagreeable odor and is so profuse that she has to change her clothes several times a day. As a result she has almost constantly a cold in her head. She has never been pregnant although she lived with her husband for twelve years; he died five years ago. Her menses stopped abruptly following a pelvic operation some ten years ago. For several years she has been always hungry. Lately she has been annoyed also by tingling and numbness in her hands and arms, and she does not see as well as formerly. The dates of onset

of her symptoms are very vague in her mind because they all developed very insidiously. Lately she has been tired constantly, but no longer suffers from headache.

One is immediately impressed by the coarseness of her features (Fig. 36). The nose is enlarged and bulbous, the lips thick, and the lower jaw projects forward. The supra-orbital ridges are very prominent and overhang the eyes. The tongue is enormous, the teeth are widely spaced,

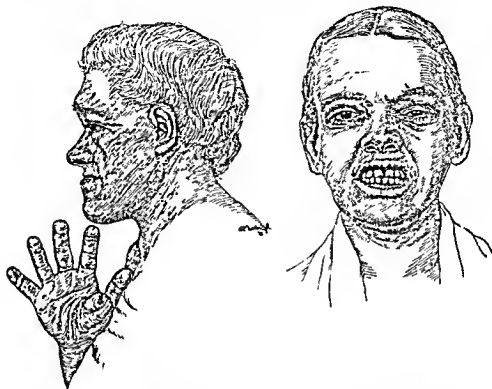


FIG. 36. Typical acromegalic patients. At the left, CASE III; at the right, CASE IV.

and the jaws are badly occluded. The skin of the face is wet with perspiration; it is coarse, with large pores and excessive hair. The hands and fingers are very broad. There is an increased amount of subcutaneous tissue so that the hands look swollen and the fingers cannot be completely flexed into the palms. The hair of the head is coarse and straight. The shoulders are stooped, the breasts flabby and pendulous. The legs are slightly bowed and the feet disproportionately large. The toes are very broad and the second toe on each foot is raised completely above its neighbors from having been confined into shoes too small.

The visual acuity is normal. The visual fields are normal although

the sella turcica is greatly enlarged in a globular manner (Fig. 37). The frontal sinuses are excessively large. The bones of the hands are broad and there are exostoses from the terminal phalanges of the fingers. A series of determinations of the basal metabolism gave an average value of +3.8 percent.

She has been treated with deep roentgen-radiation, a series of treatments being given a couple of months ago, directed toward the sella, totalling 1260R. The effect was to stop the sweating abruptly for some weeks, but now it has gradually returned. Another series of treatments

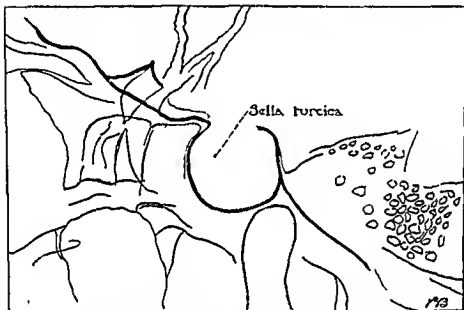


FIG. 37. Scheme of roentgenogram from CASE III showing symmetrical enlargement of the sella turcica Compare Plate II.

is in progress. Since her tumor has not yet reached a sufficient size to impair her vision it has not been necessary to perform an operation as we were obliged to do in the case of the second patient.

This woman (CASE IV) of thirty years began three years before her admission to the hospital to have headaches in the frontal region. About the same time (she cannot remember in what order these symptoms appeared) her menses ceased, her hands and feet began to enlarge, she became tired and nervous and her eyesight failed. These symptoms persisted and in addition her features coarsened noticeably. Her teeth also separated and did not close normally. She perspired a great deal, was

very nervous and had dull aches in her back and limbs. Until her present trouble she was well. She was married twice. By her first husband she had two normal children; he died when she was twenty-three years old. She married her second husband about a year later, and some four years before the onset of her present trouble, but was never again pregnant.

When admitted to the hospital the alteration of her personal appearance was at once apparent (Fig. 36). Her nose and lips were coarse, her teeth widely spaced although the under jaw did not protrude beyond the upper. The supra-orbital ridges were very prominent. Her hair was coarse and the skin of her scalp thickened and wrinkled into coarse folds.

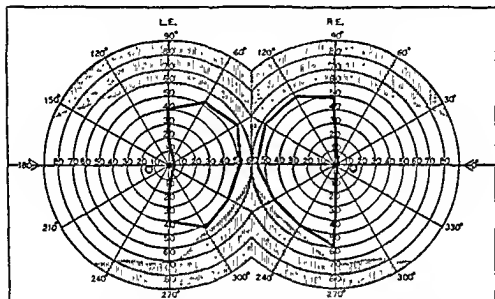


FIG. 38. Visual fields from CASE IV. Bitemporal hemianopia.

Her skin was coarse with prominent pores and always moist. Her fingers were very broad and thick, her feet enormous. Her tongue was very large and her voice hoarse. Her basal metabolic rate was $+13$. She weighed 61.7 kg. and was 166 cm. in height. Vision in her right eye was $0.8+1$ and with the left eye she could barely count fingers. There was a bilateral primary optic atrophy and bitemporal hemianopia (Fig. 38). Roentgenogram of the head showed the sella turcica to be greatly and symmetrically enlarged. The bones of the skull were very thick and the frontal sinuses enormous. The diagnosis was not doubtful. Acromegaly from pituitary adenoma was certain and, because of her already damaged vision, immediate operation was advised.

A temporofrontal flap was made on the right side; because of the large frontal sinuses and thickened skull the usual frontal extradural approach was impossible. The dura mater was opened and the frontal lobe lifted while the tip of the temporal lobe was pressed backward. Without any great difficulty the tumor was exposed bulging between the compressed optic nerves. Its capsule was opened and soft avascular tissue removed until the capsule collapsed and the pressure on the optic nerves was relieved. There was very little oozing of blood from the tumor and this was checked by a bit of muscle. The cortex of the brain appeared contused but no serious bleeding had occurred and the cortex was not ruptured. The wound was sutured carefully and the patient placed in bed apparently in excellent condition. But she did not recover well. She remained dull and drowsy. There was a paralysis of the left hand and wrist and of the left lower face. The left upper arm was unaffected, as was also the left leg. She slowly improved until on the fifth day she could move the fingers of the left hand but that evening she began to have convulsive twitching of the left facial, masseter, buccal, and lingual muscles which continued for several hours. During this time she was unconscious. Sodium luminal was given intravenously and also a solution of 50 percent glucose. The attacks ceased but she remained drowsy and sluggish for several days. The weakness of the left hand did not improve and on the tenth day the attacks recurred. She is now (two weeks later) much better and has had no more convulsions. But she is taking 200 mgm. of luminal daily. She is still very drowsy. Her basal metabolism is +9. The visual acuity is the same as on admission but the visual fields have improved slightly and her left hand has recovered its strength. There is still a lower left facial weakness.

These epileptic seizures were clearly cortical in origin and resulted either from contusion of the lower end of the precentral gyrus, due to the retraction of the brain, or else to occlusion of the middle cerebral veins which drain this region. *Paralyses and epileptic attacks are frequent sequels of operations on the hypophysis by this lateral intradural route and I never use it when it is possible to approach the tumor extradurally under the frontal lobe.*

The next patient (CASE V) was operated upon in this way several days later. Her external appearance is much different. She is thirty-three years of age and dates her illness to seven years ago when she noticed that her menses, although regular, were becoming more and more scanty and finally disappeared completely. She was married at the age of

eighteen but was never pregnant. Her husband died two years after their marriage. Until her present illness she was always well. About the same time that her menses ceased she began to suffer from severe frontal headaches. For the headaches she was given roentgen treatments and was advised to have an operation on her pituitary gland. She refused the operation and took no further treatments. For six years her condition changed but little; then gradually her vision began to fail. It was found that she had a bitemporal hemianopia. The visual acuity was



FIG. 39. At the left, CASE V; hypopituitary syndrome with wrinkled skin. At the right, CASE VI; transitional syndrome with prognathism but no other signs of acromegaly.

0.8+1 with the right eye and 0.3+1 with the left eye. She was still loath to undergo an operation, so more roentgen treatments were given. They were followed by severe headache, nausea, and vomiting which gradually improved until a second series of radiations were given four months later. Following the last treatments she suffered continuously from headache and nausea. She was very weak and sleepy and always felt cold.

When admitted to the hospital she was very feeble and remained in bed most of the time. Her face was finely wrinkled (Fig. 39) and the skin generally very delicate, dry and hairless. She weighed 49.6 kg. and was 161 cm. in height. She had never been fat. Her basal metabolic

rate was —26. Her bloodpressure was 80/60 and her temperature distinctly subnormal ranging between 36.0° and 37.2° . Her teeth were even and closed in normal occlusion. Her hands were delicate with long tapered fingers. There were no alterations of the nervous system apart from the eyes. The vision in the right eye was 0.8—2 and in the left eye 0.4—1. There was a bitemporal hemianopia (Fig. 40) and bilateral primary optic atrophy. Roentgenogram of the skull showed the sella turcica to be greatly enlarged.

An osteoplastic operation was made. The right frontal lobe was retracted and the dura mater opened along the sphenoidal ridge. The

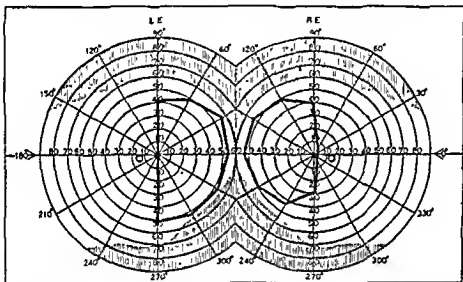


FIG. 40 Visual fields from CASE V before operation Bitemporal hemianopia.

tumor could be seen bulging between the optic nerves which were elongated and flattened. The capsule of the tumor was opened. Soft semi-liquid neoplastic tissue extruded itself through the opening. More tissue was removed by suction. There was no bleeding from the tumor. The wound was carefully closed. The patient recovered promptly. The following day she said she felt as if a pressure had been removed from her eyes. By the fourth day she could see in the temporal region of the left visual field. Her vision has continued to improve (Fig. 41) and she is ready to be discharged, fifteen days after operation.

Our understanding of the reasons for the differences in the clinical symptoms of these patients is the result of patient and persistent study of the hypophysis cerebri and of its diseases.

The DEVELOPMENT OF THE HYPOPHYSIS is known in detail (11). It arises from two primordia, one from the stomodeum and the other from the under part of the diencephalon. By the union of the two the hypophysis is made (Fig. 42). The former arises by an out-pocketing of the buccal mucosa just anterior to the oral plate to form what is known as Rathke's pouch. It extends upward and backward to make contact with the diencephalic portion, partially wrapping itself around and extending up onto the base of the brain. Its cavity, lined with ciliated epithelium, is gradually obliterated although remnants of it may remain in the adult in the form of small cysts. The posterior wall of the pouch

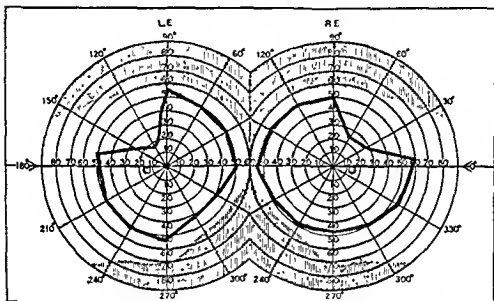


FIG. 41. Visual fields from CASE V ten days after operation. Vision recovered in temporal fields.

in contact with the diencephalic evagination is called the intermediate part of the hypophysis, while the anterior wall becomes much thickened to form the distal part. The portion which surrounds the base of the brain is known as the tuberal part. These various parts are readily recognized in the hypophysis of lower mammals such as the cat (Fig. 42), and in the human embryo, but in the human adult the intermediate and tuberal parts practically disappear. The diencephalic evagination extends downward and backward in contact with the buccal portion and is almost surrounded by the latter. Its cavity persists in some lower mammals but is completely occluded in the human adult. It is known as the neural part of the hypophysis. The buccal evagination loses its connection with the

stomodeum by the growth of the sphenoidal bone, but remnants of its neck may be found even in the adult in the posterior wall of the nasopharynx and along the craniopharyngeal canal within the sphenoidal bone. The diencephalic evagination remains always in connection with the brain by means of a long narrow stalk.

The **STRUCTURE OF THE HYPOPHYSIS CEREBRI** varies only in minor details in different mammals (20). The gland of an adult man is a

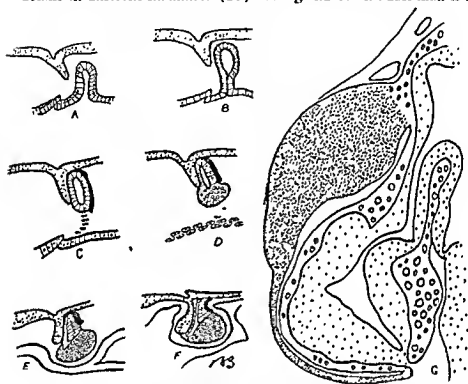


FIG. 42. A—F: development of the hypophysis. Neural part stippled, distal part indicated by circles, epithelial rest heavy black, bone unshaded. G—hypophysis of cat. Distal part heavily stippled, neural part lightly stippled, intermediate and tuberal parts indicated by circles.

small rounded structure, measuring about 6 x 10 x 13 mm. in diameter, securely buried in the sella turcica of the sphenoidal bone and covered by a portion of the dura mater known as the diaphragm of the sella. This cover is pierced by a narrow stalk which connects the hypophysis with the infundibulum of the diencephalon. The human hypophysis consists essentially of two parts, the anterior lobe and the posterior lobe, which are not readily separated as they are in lower mammals. The anterior

lobe corresponds chiefly to the distal part of the buccal evagination, with a few cells of the intermediate part surrounding small cysts near the neural portion. There are also a few cells of the tuberous part which persist along the stalk. The posterior lobe is mainly the neural portion with a few cells of the intermediate part which have invaded it.

The cells of the anterior lobe are at first small, with scanty, lightly staining cytoplasm. But about the third month of fetal life in some of the cells granules appear which stain much more heavily. These cells are called chromophile for this reason and the remaining ones are now distinguished as chromophobe. The chromophile cells are further subdivided in accordance with their reactions to stains into two classes: eosinophile (acidophile, α -cells) and basophile (cyanophile, β -cells). The two types of granules rarely occur in the same cell. The proportions of the different types of cells are roughly as follows: eosinophiles 37 percent, basophiles 11 percent, and chromophobe 52 percent. All of these cells are arranged in tortuous cords which are separated by vascular sinuses and their accompanying connective tissue. The anterior lobe, therefore, has a glandular structure and, since there is no duct, it is supposed to secrete into the vascular sinuses.

The posterior lobe, apart from the cells which invade it from the intermediate part, is composed mainly of modified neuroglial cells, the pituicytes (84). They contain granules of pigment which stain with neutral red. There is in addition a variable amount of connective tissue and a plexus of unmyelinated nervous fibers which descend the stalk from the diencephalon and end in tangles of terminals among the pituicytes. Some of them end in bulbous formations which become hyalinized so that they are clearly visible with ordinary stains and have been interpreted as collections of a secretory material. The blood-supply of the posterior lobe is scanty.

Our knowledge of the FUNCTIONS OF THE HYPOPHYSIS has increased greatly in the last few years and, although its secretion has not been identified in the blood coming from the hypophysis, there are valid reasons for believing that it is an organ of internal secretion. The nature of the evidence may be illustrated from experiments on rats.

If the hypophysis be removed from a young rat, growth is retarded (Fig. 43) and the animal does not mature sexually. If the gland be removed from a rat after the time of sexual maturity there follows a progressive loss of weight, an atrophy of the genital system, and in the female an immediate cessation of the sexual cycles, an atrophy of the

thyroid gland, parathyroid glands, and suprarenal cortex, and a general physical impairment accompanied by a lowering of the basal metabolism by about 35 percent (446). Most of these symptoms had previously been found to follow hypophysectomy in the dog (116). If now fresh hypophyseal tissue be transplanted daily intramuscularly into a hypophysectomized rat the dwarf grows at a normal rate and matures sexually, while the adult recovers his normal health, oestrus returns in the female, the sexual organs regain their normal size, and the thyroid gland and

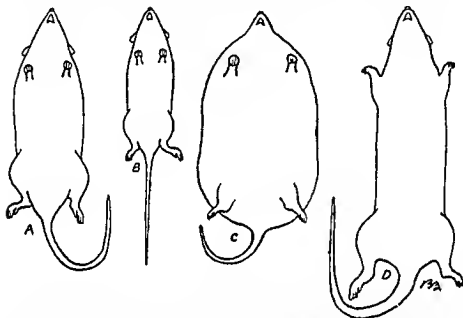


FIG. 43. Scheme showing effects of various hypophysial or parhypophysial disturbances in a litter of rats. A—control; B—after removal of hypophysis; C—after lesion in the hypothalamus D—after parenteral administration of hypophysial extract

suprarenal cortex regain their normal structure (447). It has further been shown that the continued intraperitoneal injection of an extract of the bovine hypophysis into rats causes them greatly to exceed their litter-mates in size producing thus veritable giants (186). When similar continuous injections are made into dogs there result symptoms resembling those of our first patient, namely, enlargement of the acral parts, polyphagia, asthenia, sialorrhea, and spontaneous lactation (390). When such an animal is examined after death there is found also skeletal overgrowth, hyperostoses, and a generalized splanchnomegaly affecting most strikingly the thyroid gland and genital tract. There are also

adenomas in the suprarenal glands, the thyroid gland is hyperplastic, and the ovaries contain ripe but unruptured follicles. These pathological alterations resemble closely those of the acromegalic syndrome in man.

The inference is clear that *the symptoms resulting from removal of the hypophysis are due to removal of some substance (or substances) in the hypophysis*. Since the removal of the posterior lobe alone causes none of the symptoms the causative substances must be within the anterior lobe. Extracts of the bovine hypophysis will repair the growth-defect of hypophysectomized rats but will not repair the damage done to the glands of internal secretion. This latter fact seems to point to the presence of two hormones, at least, one promoting growth (called phyone) and another (hebin) acting on the gonads. Extracts having a definite action on the genital organs have been prepared from the hypophysis of the sheep (491). The presence of a separate substance (or substances) acting on the gonads is indicated by other experimental evidence. For example, transplants of anterior hypophysis into immature animals will cause precocious sexual maturity. The action of the transplants must be indirect by intermediation of the gonads because the effect is not obtained in spayed or castrated animals. No such effect is produced by the growth-producing hormone; there must be another hormone which has been called hebin (178). Numerous other substances have been extracted by chemists from the anterior lobe of the hypophysis; that they are hormones has not yet been proved.

The foregoing anatomical and physiological data are necessary for the understanding of adenomas of the hypophysis. These tumors arise always from the anterior lobe; tumors of the posterior lobe of the hypophysis are unknown. }

ADENOMAS vary in size from a few millimeters to five or six centimeters in diameter. They arise most commonly near the stalk. In this region chromophobe cells predominate and this probably accounts, in part, for the fact that the cells of hypophysial adenomas are predominantly chromophobe (171). Adenomas composed of basophilic cells occur only as microscopical lesions. The occasional reporting of a basophilic adenoma of large size is an error due to the fact that the chromophobe cells stain more heavily with hematoxylin than with eosin. The so-called pituitary "basophilism" is a polyglandular syndrome, whose exact etiology is uncertain (297). There remain, therefore, only chromophobe and eosinophilic adenomas which are known certainly to cause clinical symptoms. Grossly there is no difference in the appearance of a

chromophobe and an eosinophilic adenoma. However, as a general rule, the eosinophilic tumors are smaller in size and appear to grow more slowly. Such an adenoma when sectioned has a smooth pinkish-gray surface with few large bloodvessels (Fig. 44).

✓ In its growth the adenoma first compresses the hypophysis which is usually found flattened almost beyond recognition in the depths of the sella turcica. At times microscopical examination is necessary to find the remnant of the gland which is stretched in a narrow band around a considerable part of the circumference of the tumor. The dural covering

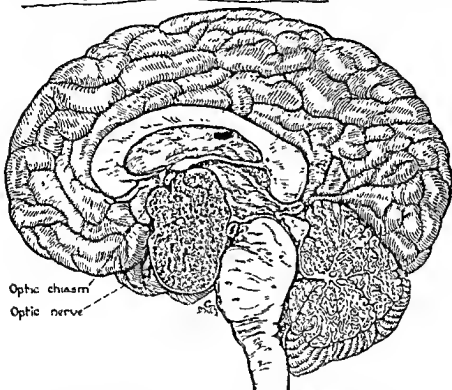


FIG. 44. Median section of brain with hypophysial adenoma in place. Note the relationship of the optic nerve and chiasm to the tumor.

of the sella turcica and the sella itself are more resistant but both finally yield. The sella turcica is enlarged in a typical manner, like the enlargement of a distended balloon (cf. Fig. 37). Usually the dural covering yields before the floor of the sella turcica is completely perforated so that the under surface of the tumor, although it projects downward into the sphenoidal sinus, is covered by a thin shell of bone. But it may penetrate the bone and fill the sphenoidal sinuses, even appearing in the

nasopharynx. The covering of the sella turcica usually yields anterior to the optic chiasm which is pushed upward and backward by the expanding lesion, the optic nerves anterior to the chiasm being elongated and flattened.

The growth may project posterior to the chiasm or laterally, indenting the uncus. In some instances the tumor may insinuate itself between the dura mater and the base of the skull, spreading widely in the temporal fossae. Or, instead of remaining more or less globular in form after penetrating the covering of the sella, it may spread irregularly, sur-

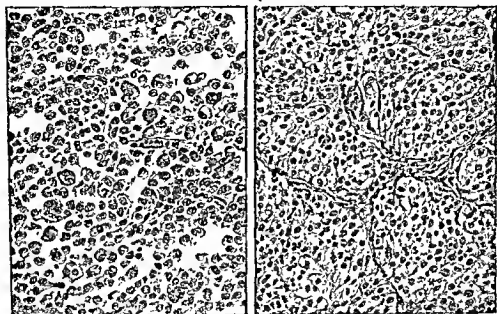


FIG. 45. Drawings of microscopical preparations of hypophysial adenomas. At the left, a chromophile adenoma of acromegaly; at the right, a chromophobe adenoma.

rounding the internal carotid arteries, projecting into the cavum Mecklii or through the incisura tentorii into the cerebellar fossa. Usually, however, the adenoma remains more or less globular, deeply indenting the diencephalon anterior to the optic chiasm.

HISTOLOGICALLY two distinct types of adenoma may be distinguished, with many transitional forms. The most common type is composed of chromophobe cells (Fig. 45). The cells are polygonal or slightly elongated and tend to be arranged roughly into large groups by a more or less developed stroma proliferated from the numerous thin-walled vascular sinuses. When the stroma is less abundant the cells may

seem to radiate around the vessels. The cytoplasm of the cells is delicate and stains lightly with eosin. Numerous small granular mitochondria are present but no other granules. The nuclei are oval with abundant chromatin; many pyknotic types are seen, but rarely mitoses. In the eosinophilic adenoma (49) the cells lie in a loose mass without stroma (Fig. 45), and with few vascular sinuses. The cells tend to be rounded and vary greatly in size. The nuclei also vary in size and many multinucleated cells are present. The nuclei also often lie eccentrically in the cytoplasm, which may undergo a hyaline transformation in the central part. Because of the poor blood-supply these tumors are often necrotic. But most important is the fact that with proper staining there may be demonstrated, usually in the periphery of the cytoplasm but often throughout the cell, innumerable fine granules which stain like the eosinophilic granulation of the normal hypophysis. The granules are, however, smaller in size often making a sort of fine dust in the cell. Between these two extremes of structure all sorts of transitions may be identified (47).

If now the clinical symptoms be correlated with the histological structure of the adenoma it is found that *the presence of eosinophilic granulation is always associated with signs of acromegaly and that the intensity of the acromegalic syndrome varies with the intensity of the eosinophilia, other things being equal.*

ACROMEGALY is a rather rare, non-hereditary but sometimes familial, clinical condition which begins any time between the ages of fifteen and fifty years. The most common age of onset is the decade between twenty and thirty (130).

The most frequent symptom, and usually the first to be remarked by the patient, is an increase in size of the acral parts—hands, feet or jaws. The palm becomes broadened and the fingers likewise, making the whole hand appear square and shortened. At the same time the soft tissues become thickened so that the hand and fingers feel stiff and swollen. The patient's attention may be attracted to the change by difficulty in putting on his ring or by the necessity for a larger size of glove. The same transformation affects the feet so that he must wear an ever increasing size of shoes. Simultaneously he (or his friends) notes that the appearance of the face is changing; the features become coarse, the lower jaw prominent and the teeth close badly. Although these changes are most evident in the acral parts the entire body is involved in the overgrowth. There is a stoop to the shoulders, the skin is thickened and coarsely wrinkled, especially over the scalp. There may be a general

overgrowth of hair. All of these alterations may progress steadily until a veritable caricature results, well known in the comic theatet for centuries. If the disease begins so early that the epiphyses are not yet closed the patient may grow also in height to become in some cases really gigantic.

Other early symptoms are headache, and in women disturbance or cessation of the menses. In fact the alteration in external appearance is often so insidious that the patient's attention is first called to it by the physician whom she consults for other symptoms. The headache is a dull aching pain in the temporal region. Although sometimes the menses may continue in spite of the advancing disease, in almost all cases they become irregular and finally cease; pregnancy then becomes impossible.

Somewhat later other symptoms appear. The patient has a feeling of fatigue, loses interest in his work, becomes depressed and may become dyspneic on exertion. The male loses his libido sexualis and may even become impotent. Excessive sweating occurs and the perspiration has a disagreeable odor. The patient is always hungry and eats voraciously. He may also have a polyuria and increased thirst; if examined at this stage he is often found to have a glycosuria and his basal metabolism is elevated. The patient complains also of paresthesias, and even of pains of neuralgic character, throughout the body.

After many years the headaches may suddenly cease and about the same time a new train of symptoms appears, headed by disturbances of vision. The cessation of the headache is supposed to coincide with the rupture of the diaphragma sellae by the expanding tumor. This usually occurs anterior to the optic chiasm and between the optic nerves. The resulting defect in vision will be obvious from a study of Figure 21. The tumor presses first on the lower crossed fibers of the chiasm, arresting their function and ultimately causing them to atrophy, thus producing a bitemporal hemianopia which begins in the upper quadrants of the visual fields (144). When the visual defect has progressed toward a complete bitemporal hemianopia the patient becomes conscious of his defect. He has then difficulty in reading and a tendency to bump objects or people approaching him from the side. The macula is finally encroached upon and the visual acuity diminishes. In a few instances the tumor may project lateral to the chiasm; a homonymous hemianopia then results. Rarer symptoms of pressure on nervous structures may be present. The patient may have epileptic attacks preceded by a disagreeable odor or taste; these are evidences of involvement of the uncus. He

✓ may become sleepy and lethargic from involvement of the hypothalamus. ✓

Enlargement of the sella turcica is found in over 90 percent of acromegalic patients but in nearly a third of them the tumor never reaches sufficient size to cause visual disturbances and the other late symptoms we have just described. In fact a few well-authenticated records exist in which there was no tumor of the hypophysis, but rather a hypertrophy of its anterior lobe, or general eosinophilia of its cells.

Many acromegalics attain great stature, and it has long been known that giants have many evidences of the alterations which we have just described as acromegalic. Sufficient evidence exists to prove that acromegaly and gigantism are closely allied, and all transitions between the two conditions may be found. If the disease sets in before the epiphysial lines are closed, a giant results, but if the disease begins after their closure, an acromegalic syndrome results. Sooner or later in the course of most acromegalics another phase appears. The sweating ceases; the skin loses its coarseness and the hair falls out; the thickness and puffiness of the subcutaneous tissues diminish; the polyphagia, polydipsia, and glycosuria cease; the patient becomes more asthenic than ever. If his basal metabolism is determined it is found to be markedly subnormal. This same transformation has been found to occur when a large part of the tumor has been removed at operation or following intensive roentgen-radiation. But the bony changes persist unaltered. The significance of this final phase we will discuss presently (p. 108).

It sometimes happens that a patient with a pituitary adenoma will have very slight signs of acromegaly—a little thickening of the features, a slight progoathism, or a normal or slightly elevated metabolism. Such cases are known as fugitive acromegaly (47). Only a few eosinophilic cells are found in these tumors. The next patient is an excellent example of this condition.

He is a man (CASE VI) of forty-three years, who dates his illness from ten years ago but, previous to that, in the army, he had begun to have difficulty in sighting his gun. At any rate, about ten years ago he began to have headaches in the frontal region. These grew worse and for the last five years have been very severe. He had his glasses changed very often during this time without much relief. For the last four years he has been unable to focus his binocular and has noted that he had trouble reading the left-hand side of a page. His vision finally became so bad that he was unable to do his work as a bookkeeper and came to the hospital for relief. He had previously been well except for a

nephritis with hypertension some years previously. He was unmarried but insisted that there had been no diminution of either libido or potency.

When admitted to the hospital his appearance was not suggestive. He was tall and well formed, 181 cm. in height, and weighed 74.8 kg. His features were regular and his skin normal. His hands were long and well shaped. But his chin was prominent (Fig. 39), and when his teeth were inspected it was seen that the lower ones closed anterior to the upper ones. He does not remember any period of malocclusion but thinks his teeth have always been so. Skin and distribution of hair were normal. His genitalia were of normal size. Aside from a slight prognath-

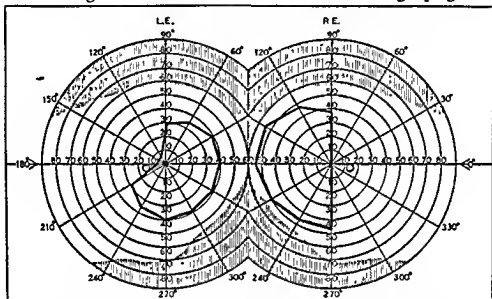


FIG. 46. Visual fields from CASH VI. Note the upper quadrantic defect in the left temporal field.

ism very little abnormal could be found in his external appearance. His blood-pressure was 120/80 and his temperature normal. His basal metabolism was -19 . His vision was very poor in the right eye ($0.3+1$) but practically normal in the left (1.5). There was a primary atrophy of the right optic nerve; the left appeared quite normal. There was a temporal hemianopia of the right eye, and an upper outer quadrantic defect in the left visual field (Fig. 46). Roentgenogram of the skull showed the sella turcica to be greatly and symmetrically enlarged. The diagnosis was made of adenoma of the hypophysis with some slight signs of acromegaly. Immediate operation was advised.

A transfrontal osteoplastic operation was made. The right frontal lobe was elevated and the dura mater opened along the sphenoidal ridge.

The tumor was seen bulging between the greatly flattened and elongated optic nerves. Its capsule was opened and rather firm neoplastic tissue was removed with a dull curette until the compression of the optic nerves was relieved. There was oozing of blood from the cavity which was checked by packing with cotton and finally by insertion of a bit of muscle. The patient recovered promptly. His vision improved and he was discharged twelve days after operation. It is now five weeks later and he has returned to work. Visual acuity of the right eye has increased to 0.8 and the lower part of the temporal field has filled out. The acuity of the left eye is 1.5+1, the visual field is of normal contour, but with a large relative paracentral scotoma.

✓ When the body of a pronounced acromegalic patient is examined post-mortem there is found everywhere a most amazing overgrowth of tissues (142). It is most evident in the bones and connective tissues, but the splanchnomegaly is also striking. The alterations of the bones have been most carefully described (293). The change in the lower jaw is one of the most obvious. The width between the lower molars is increased; the canines are advanced, the porous vascular bone is heaped up on the alveolar margins. The whole lower jaw is pushed downward and forward by growth at the temporomandibular joint. The region of the angle is absorbed and increased growth also occurs at the mental eminence, so that the total effect is to open out the angle between the body and ramus. The lower jaw finally projects markedly beyond the upper one. Other changes occur in the skull. The whole outer wall of the orbit is moved forward and the zygoma downward. The insertion of the temporal muscle is much more extensive than normal. There is an immense growth and thickening of the supra-orbital region and between the insertions of the temporal muscles. The occipital muscles acquire a greater area of insertion and the external occipital protuberance is enlarged. Similar changes take place elsewhere in the skeleton; wherever muscles and ligaments pull upon the bones, growth takes place. Veritable exostoses may be produced at these points. Atrophy also takes place in the cancellous bone, the resulting weakness causing kyphosis and flat feet. Exostoses occur also at the ends of the terminal phalanges of the hands and feet.

The connective tissue of the body is increased in amount, especially around the nerves. This, together with the exostoses, explains the neuralgic pains from which these patients suffer. The increase in the connective tissue of the skin is definite but there seems also to be an admix-

ture of edema which in part causes its turgidity and stiffness. The splanchnomegaly is general. The lungs are about twice normal weight; the heart may reach a weight of 1275 grams and death from cardiac failure is common; the liver averages nearly twice normal weight; the kidneys are uniformly hypertrophied; the spleen varies greatly, but is usually enlarged also. Whether the splanchnomegaly is caused by an increased number of cells in these organs, an increase in the size of the individual cells, by increased blood-supply, or otherwise has not been finally decided. The alterations in the endocrine glands are more varied. We have already noted the rare hypertrophy and more common eosinophilic adenomatous transformation of the hypophysis. The thyroid gland is usually enlarged, adenomatous, of colloid type, without histological evidence of toxicity in spite of the increased metabolic rate which some have interpreted as evidence of increased activity of the thyroid gland. The alterations of the parathyroid glands have not been carefully described; they are occasionally at least enlarged and in one case an adenoma was found. The thymus often persists and may reach a weight of as much as 78 grams. Hypertrophy of the adrenal glands is common; adenomas are found in the cortex. The pancreas also is greatly enlarged, the islands being often particularly hypertrophic. The changes in the testes and ovaries have not been clearly established. What can be the explanation of these amazing alterations? The answer lies in what we have already learned concerning the function and pathological alterations of the anterior lobe of the hypophysis. In acromegaly there is almost always present an adenoma consisting of cells containing the eosinophilic granulation of the normal anterior lobe. The only exceptions are the few cases of hypertrophy of the hypophysis in which there is a great increase in the number of eosinophilic cells. We have already seen that gigantism may be produced in rats by injecting intraperitoneally into them extracts of the anterior lobe over a long period of time; in this animal the epiphyses never close. In a similar manner, symptoms of acromegaly have been produced in a dog. In this animal the epiphyses do close. *The inference is unescapable that these syndromes in man are due to a hyperfunction of the eosinophilic cells of the anterior lobe of the hypophysis; whether gigantism or acromegaly develops depends upon the age of onset of the disease.* The cells of the eosinophilic adenoma must continue to function in a manner approaching normal.

The third patient whom I showed you has just as surely a HYPOPITUITARY SYNDROME due to suppression of at least some of the function of

the anterior lobe of the hypophysis. The symptoms of hypophysial deficiency also vary with the age of the patient. The hypophysis is rarely destroyed in children by an adenoma, but the symptoms resulting from its destruction are well known from the results of other lesions. We may use, as an illustration of what should result from a destructive lesion confined to the anterior lobe of the hypophysis in childhood, the examination of a male dwarf aged twenty-one, who died of meningitis following otitis media (440). He was well proportioned and moderately nourished, but only 111 cm. in height. In very early childhood he had some illness after which he did not grow. The beard, and axillary and pubic hair were absent. The external genitalia were those of a baby. The testes weighed 0.9 and 1.2 gms. respectively; microscopically their structure was similar to that of a baby's testes. The thymus weighed 2.5 gms.; the adrenal glands 2 gms.; the thyroid gland 2 gms. Histologically the thyroid gland, adrenal glands, pancreas, liver, and spleen were normal. The hypophysis weighed 0.2 gms. The posterior lobe was normal, but in place of the anterior lobe were found several small cysts and only traces of abnormal glandular tissue. In the clinic, children always present a mixture of the hypopituitary with the hypothalamic syndrome. The differentiation of the latter will be discussed later (p. 126).

We will confine our attention now to the hypopituitary condition as it appears in the adult (171). In a typical case the general symptoms which the patient notices are lassitude, lack of energy, sensitiveness to cold, impotence in the male or cessation of the menses in the female, dryness of the skin, and loss of hair. When such a male patient is examined one is immediately struck by the alteration in his general appearance. The skin is smooth, delicate, and of a pasty color. The bodily hair is much reduced and may be confined to the pubic region where it has a feminine distribution. Axillary hair is absent or scanty and the beard is very slight. The body is usually said to be feminine in contour; it is much more exact to say that its contour is infantile. Both in the male and female there is a tendency toward the indifferent infantile type. The skin is, moreover, covered with delicate wrinkles especially evident in elderly patients over the face and neck (Fig. 39).

In more severe cases there is progressive emaciation (441) (Simmond's disease), the characteristic findings being a senile appearance, the loss of teeth, the disappearance of the menses, the loss of axillary and pubic hair, and a chronic otherwise inexplicable emaciation. At necropsy one notes the wrinkling of the skin of the face, the splanchno-

micria affecting liver, spleen, adrenal glands, genitalia, ovaries, heart, and kidneys. Such severe symptoms rarely, if ever, accompany hypophysial adenomas. In the early stages also, when the hypothalamus is compressed before severe destruction of the hypophysis has occurred, adiposity is present in variable degree, more frequently in young adults. In the female the absence of hair is not so evident, but the infantile or adolescent bodily configuration is common, and cessation of the menses is an early and constant finding. Examination in the laboratory discloses a marked lowering of the basal metabolism, the readings often being as low as -30 (141). The difficulty in oxidizing glucose, so often remarked, is probably one phase of a general lowering of metabolism.

These symptoms of hypofunction of the hypophysis (anterior lobe) we recognize as those which we have already remarked in the terminal stages of an acromegaly, when the eosinophilic adenoma is extensively destroyed by degeneration or hemorrhage.

Aside from the symptoms due to alteration of the function of the hypophysis, which we have just described, an expanding adenoma causes other symptoms by pressure on adjacent nervous structures—*neighborhood symptoms* (130). We have already described the headache which is supposed to be caused by distension of the dura mater over the sella turcica. The headache is usually bitemporal but may radiate to the frontal region or behind the eyes. The sella turcica is eroded by the expanding growth in a symmetrical manner, like a distended balloon, from its normal dimensions (10-12 mm. anteroposteriorly by 14-15 mm. in width and 8 mm. in depth) to as much as 2.5 cm. in every diameter. As soon as the diaphragma sellae yields, the expanding tumor presses upon the optic chiasm, usually projecting upward between the optic nerves anterior to the chiasm. The inner inferior part of each optic nerve is thus first pressed upon. The result, as I have already noted, is a defect in the upper outer quadrant of each visual field. As the pressure continues there follows a complete bitemporal hemianopia, then the lower outer quadrant of each visual field is involved, and finally complete blindness ensues. The progression in the nasal half is not so regular and the final island of vision may be in the lower quadrant of the nasal field. When the pressure on the chiasm is relieved, the process is to a certain extent reversed, but the macula recovers much more slowly and incompletely so that a central scotoma may remain indefinitely. The fundus oculi presents the typical picture of a primary optic atrophy. The optic disc is white and clearly outlined; the lamina cribrosa clearly evident. Only in

rare cases does the intracranial tension rise sufficiently to cause a choked disc.

As the tumor continues upward it presses upon the diencephalon and adiposity results. Later somnolence is a prominent symptom, but this is doubtless partly due to the lowered metabolism. It is strange that a polyuria rarely occurs — one of the most common symptoms of injury to the hypothalamus. When the tumor projects laterally to the chiasm there may result a homonymous hemianopia and, from pressure on the adjacent uncus, so-called uncinate seizures with gustatory or olfactory aura. Late in the course of the disease anosmia from involvement of the olfactory tract, pain in the trigeminal area, mental disturbance, hydrocephalus, and increased intracranial tension may complicate the clinical picture.

A DIFFERENTIAL DIAGNOSIS of hypophysial adenoma must be made from all other conditions giving evidence of altered hypophysial function. We have already pointed out that, with the exception of a rare case wherein there is a tremendous increase in the number of eosinophilic cells in the anterior lobe without much increase in its size, acromegaly is always associated with an adenoma. The presence of an adenoma in an acromegalic patient may be verified then by roentgenogram of the sella turcica.

Evidences of loss of hypophysial function are caused by numerous lesions aside from adenoma. Absence of enlargement of the sella turcica will almost rule out an adenoma; very rarely an adenoma will leave the sella turcica before enlarging it and in these cases the diagnosis is not possible to establish with certainty, in the absence of acromegaly. In case the sella is eroded the adenoma must be differentiated from other tumors in the neighborhood, notably from the glioma of the optic chiasm and the craniopharyngioma. Both of these tumors occur principally in children, whereas the adenoma is distinctly a tumor of adults (Fig. 47), usually young adults, and almost never occurs under the age of fifteen. In neither of the other tumors is the progress of the defect in the visual fields so regular. The deformation of the sella turcica is different also in the three tumors. The adenoma balloons the sella; the craniopharyngioma erodes it irregularly; with the glioma of the chiasm there is an excavation under the anterior clinoidal processes. The glioma of the optic nerves causes enlargement of the optic foramina, visible in the roentgenogram. The craniopharyngioma is often calcified, the others very rarely. The glioma and craniopharyngioma are often accompanied

by polyuria, the adenoma rarely, if ever. When the sella turcica is not enlarged or eroded, the adenoma must be differentiated from other tumors causing bitemporal defects in the visual fields. Chief among these are the meningioma of the tuberculum sellae and the craniopharyngioma (123). It is perhaps impossible always to differentiate them, especially when the craniopharyngioma is in an adult and not calcified.

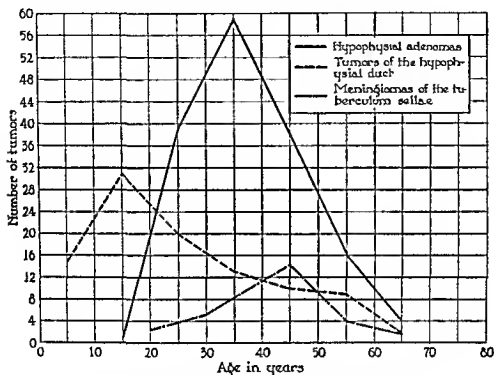


FIG. 47. Graph illustrating the difference in age-distribution of hypophysial adenomas and tumors of the hypophysial duct.

Since there is at present no effective form of glandular therapy available for the cure of hypophysial deficiency in man, the TREATMENT of hypophysial adenomas is reduced practically to relief of the neighborhood symptoms, notably failure of vision. The effect of treatment can be most adequately controlled by examination of the visual fields. The growth of an adenoma can sometimes be retarded and even a regression in size obtained by persistent roentgen-radiation (471). This observation has been often repeated and certainly, if there is no immediate danger to vision, roentgen-radiation should be tried in every case. It should not be forgotten, however, that serious accidents may occur,

notably from edema or from hemorrhage into the tumor, immediately after too energetic radiation. In either case vision rapidly fails and prompt operation is necessary.

At operation the main problem is to decide how much of the tumor to remove. Complete removal is rarely possible and never advisable. It is impossible at operation to distinguish tumor from the small portion of normal gland remaining; if this remnant is removed a pituitary insufficiency may be greatly exaggerated and for this condition, as we have already noted, there is no efficient treatment. It has been repeatedly demonstrated that, after operation for acromegaly, certain acromegalic signs and symptoms recede (137). But it should also be pointed out that too radical excision of the tumor may be followed by a pituitary insufficiency still more disastrous for the patient than his acromegaly. Perhaps these risks may best be avoided by keeping constantly in mind that the sole indication for treatment, with the possible exception of the early active stage of acromegaly, is to save vision. If this can be done with roentgen-radiation, well and good; if not, operation is necessary. But in both cases treatment is to be restricted to what is necessary to preserve vision in the fear of exaggerating the hypophysial deficiency.

CHAPTER 6

CRANIOPHARYNGIOMAS

SYNDROME OF THE HYPOTHALAMUS

We have learned how, following the description by Marie of the clinical entity which he called acromegaly, it was pointed out that this syndrome was associated with a tumor of the hypophysis cerebri. It was immediately concluded that the disease resulted from destruction of the gland. But clinicians were soon puzzled by the reports of tumors in this region which caused no symptoms of acromegaly. Some early reports by Mott, by Babinski, and by Froelich concerned cystic epithelial tumors. Mott in 1899 suggested their origin from the hypophysial duct (350). An exhaustive study by Erdheim in 1904 established the essential characteristics of these particular intracranial neoplasms. They have many synonyms — suprasellar cysts, tumors of Rathke's pouch, hypophysial duct tumors, adamantinomas, ameloblastomas, epitheliomas, etc. Many of these terms are unwieldy; others are inexact. It is generally conceded that they are epitheliomas and that they arise from squamous epithelial rests of the craniopharyngeal duct. We shall, therefore, speak of them as epitheliomatous tumors of the hypophysial duct, or briefly as *craniopharyngiomas*. I have two young patients to show you which will give you a notion of the sort of clinical syndromes caused by the craniopharyngiomas.

The first boy (CASE VII) is now sixteen years old. He began at the age of six to have attacks of pain over the left eye. They came at long intervals but were severe enough to keep him in bed. At the age of ten there was a serious bout of almost constant headache lasting nearly four weeks, during which time he vomited frequently. Since then the headache has been less frequent and less severe. At the age of eight his eyes were examined by an oculist and glasses prescribed, but it was not until two years later that he complained of difficulty of vision. He then noticed blurring and that he could not see to the left with the left eye. Enuresis continued to the age of nine. Since the age of ten at least he drank excessive amounts of water and had to get up at night to urinate. During all his life he had recurrent attacks

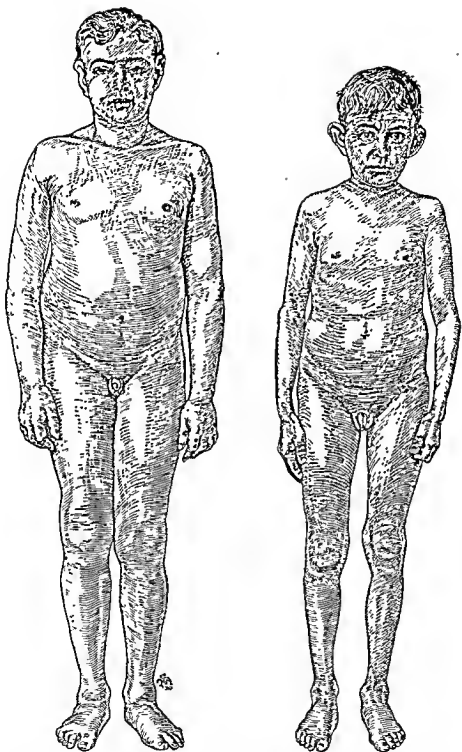


FIG. 48. Patients with craniopharyngiomas. At the left, CASE VII; at the right, a patient thirty years old with a strange mixture of infantilism and senility.

of vomiting accompanied by epigastric distress. He also had frequent fainting spells, the last one five years ago during which he lost consciousness for the first time, but later he improved so that he seemed a normal boy except that he was possibly slightly underdeveloped.

When examined in another clinic four years ago there were no evidences of puberty. The genitalia were small but the testes were descended. His height was 145 cm. and weight 41.0 kg. His basal metabolism was -34 . There was no definite polyuria; the intake of water averaged only 2000 ccm. daily. There was a primary optic atrophy in each eye. In the left visual field was a temporal hemianopia; in the temporal half of the right visual field was a large scotoma. The visual acuity was 20/100 in the left eye and 20/100 also in the right. A roentgenogram of the skull showed the pituitary fossa to be enlarged and just behind and above the anterior clinoid processes were a few small areas of calcification.

At that time, four years ago, a right transfrontal operation was performed elsewhere, the scar of which is plainly visible to you. The right optic nerve was found to be flattened by a bulging tumor to the left of it. The tumor was punctured and proved to be cystic. A bloody fluid containing numerous crystals of cholesterolin was withdrawn; the optic chiasm was then seen to be anterior to the cyst. The cyst was adherent to the surrounding structures; a few fragments of its wall were removed. Their microscopical structure was that of a typical craniopharyngioma. There was an immediate postoperative polyuria of eight to nine liters daily which was reduced by subcutaneous injections of pituitrin to 2500 ccm. There was no postoperative hyperthermia. Within a month the left vision was 20/70 and the visual field had enlarged in the upper temporal quadrant. He could barely count fingers with the right eye. He gained rapidly in weight and the polyuria continued, fairly well controlled by a nasal spray of pituitrin.

He is now, four years after operation, 157 cm. in height and weighs 54.1 kg. His basal metabolism is -27 . His temperature varies daily from 36.4° to 37.8° . His output of urine is 7700 ccm. daily when not controlled by pituitrin. His genitalia are still very small and his body hairless and infantile (Fig. 48). The turgor of the subcutaneous tissue, the fineness of the skin, and the childish contour of the body are all evidences of infantilism. There have been no signs of puberty—no erections and no nocturnal emissions. The visual acuity of the right eye is 0.1 and of the left eye 0.4—1. There is a large paracentral scotoma

in the temporal half of each visual field (Fig. 49).

The other boy (CASE VIII) is only seven years old. He has always been thin and undersized. Since the death of his mother he has lived in an orphanage. He began a year ago to complain of headache and vomited frequently. When examined at this time he was found to be very alert and very religious, talking a great deal and asking foolish questions. A lumbar puncture was made after which he was stuporous

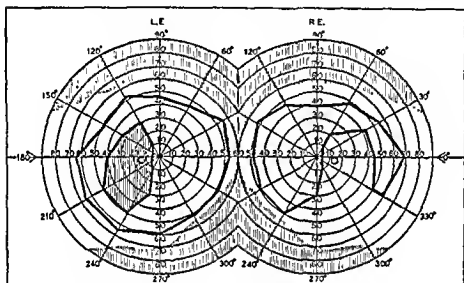


FIG. 49. Visual fields from CASE VII.

for some time. The lower extremities were spastic. The optic discs were pale. The visual fields were not examined. The sella turcica was seen in the roentgenogram to be elongated and the dorsum was depressed. He improved after a while, stopped vomiting and appeared normal for five months. He then began to walk haltingly, feeling his way about. Three months afterward he became incontinent, was listless and drowsy. Soon he became blind in the right eye, and began again to have severe headache and vomiting. At this time he was taken to a children's hospital. There he was found to have bilateral exophthalmos, to be blind in both eyes, and spastic in all his extremities. He was unable to walk without assistance. The head was retracted. The optic discs were choked. The father was advised to bring him to this clinic and did so a month ago.

He arrived stuporous. Both pupils were dilated and reacted sluggishly to light. The optic discs were elevated about three diopters with numerous hemorrhages. Both eyes were blind. There was a "cracked-pot" resonance when the head was percussed. All of the limbs were spastic but the left ones more so. There was a marked tremor of both hands. In the roentgenogram there could be seen a spotty calcification above a dilated and eroded sella turcica. The child had been blind so long that no hope was entertained of recovering his vision. His

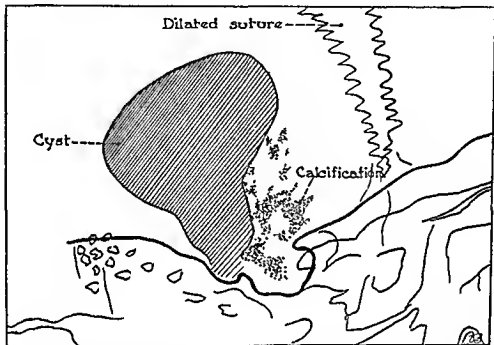


FIG. 50. Scheme of roentgenogram from CASE VIII showing relation of cyst and tumor to the sella turcica. Compare Plate III.

general condition was so very bad that operation offered little hope of recovery, so a lumbar-puncture needle was inserted between the dilated sutures of the cranium and a cyst was punctured above the sella turcica from which seventeen ccm. of yellow fluid, containing numerous crystals of cholesterolin, were withdrawn. The cyst was then filled with air and a roentgenogram was again made (Fig. 50) which shows well the situation of the tumor. The child's condition improved immediately and he is now very alert mentally and plays about the ward normally. His daily output of urine is normal. His weight is 20.4 kg. His height is 109 cm. His genitalia are fairly normal for his age and his general

habitus, although delicate, is not abnormal. The only abnormality which one notes is a strange senile appearance of the facial expression. It might readily be overlooked in this boy but in some cases the strange mixture of infantilism and senility makes a queer impression (Fig. 48).

In this latter patient we miss many of the symptoms of the first one, notably polyuria. The genital dystrophy will doubtless become apparent at puberty if he lives to that age. I do not contemplate operating on him now but will wait to improve his general condition in the interval before the cyst refills and his symptoms of increased intracranial tension recur. I regret only that it is now impossible to save his eyesight.

The customary GROSS STRUCTURE of the craniopharyngioma justifies the therapeutic procedure adopted for the second boy. Such a tumor is almost invariably cystic, especially when it has reached such a size. For this reason it is often spoken of loosely as a suprasellar cyst. It lies above the sella turcica projecting downward into it and extending upward into the third ventricle, often completely filling the latter and pressing upon its walls in every direction. The smaller tumors may rarely be solid. These tumors may arise either above or below the diaphragma sellae. The subdiaphragmatic tumor compresses the hypophysis but does not usually balloon the sella. Instead it erodes the sella irregularly, the dorsum suffering mainly. It then projects upward, usually anterior to the chiasm but often posterior to it or even to one side. The supradiaphragmatic tumor projects upward into the third ventricle and may come early to lie above the optic chiasm, which it compresses downward and forward. The hypophysis is also flattened in the bottom of the sella turcica, and the dorsum sellae and anterior clinoidal processes are eroded (Fig. 50).

The alterations of the sella turcica are quite variable (64); it may even appear to be completely normal. Usually some abnormality is found but rarely is the ballooning produced so characteristic of the hypophysial adenoma. Often both the anterior and posterior clinoidal processes are partially or wholly eroded. Again there will be only absorption of the dorsum sellae. Because of these erosions the sella appears shallow and its anteroposterior diameter increased. The hypophysis is usually to be found as a flattened crescentic body in some part of the floor of the sella, but in rare cases may be mainly on top of the tumor; it is usually impossible to make out its various parts and the stalk is rarely discoverable. In many instances the hypophysis is to be found only by

microscopical examination. Rarely it will be only slightly flattened or completely normal.

The tumor has a smooth or grossly nodular surface which usually projects into the cavity of the third ventricle without any capsule either of neuroglia or connective tissue. It may sometimes be peeled away from the surrounding nervous structures and has few vascular connections with them. It is attached below to the region of the sella tur-

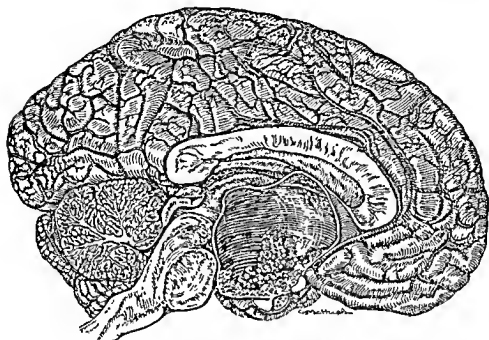


FIG. 51. Median section of brain with craniopharyngioma in place

cica and at operation it should not be forgotten that somewhere on its anterior surface the anterior communicating artery will be found. The arteries of the *circulus arteriosus* also lie in close apposition to its basal parts and in fact may be imbedded within them. The smaller tumors are often solid, perhaps all of them are in the beginning, but usually cystic cavities are present and vary in size from those visible only with the aid of the microscope to others four or five centimeters in diameter. The larger cysts are found to contain a viscid fluid varying in color from a light yellow to a greenish black. The fluid does not clot when exposed to the air. It contains almost always numerous crystals of cholesterol which are visible to the naked eye as shining spots on the surface. The solid part of the tumor usually lies in the neighborhood of the sella with the cyst above. The wall of the cyst may be very thin and contain no evi-

dence of tumor, or again, papilliform excrescences may be seen here and there (Fig. 51). It insinuates itself everywhere and may project through the foramen interventriculare into the lateral ventricle or through the incisura tentorii into the cerebellar fossa. Usually, however, it remains confined to the third ventricle. The obstruction of the third ventricle interferes with the freedom of circulation of the cerebrospinal fluid so that there is usually more or less internal hydrocephalus from dilatation of the lateral ventricles. The corpus callosum is elongated and

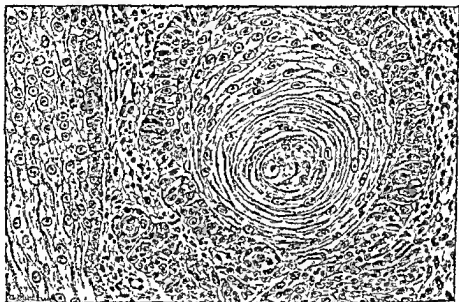


FIG. 52. Microscopical drawing of craniopharyngioma.

thinned and there are often openings of considerable size in the septum lucidum.

The MICROSCOPICAL STRUCTURE is composed essentially of epithelial cells which vary, however, greatly in appearance. Sometimes there seems to be a more or less continuous sheet of cytoplasm in which the nuclei are embedded. More often the cellular boundaries are distinct and intercellular bridges are found (Fig. 52). Still more frequently the cells are columnar, especially along the connective tissue. The last type is often called adamantinomatous (115) because of its resemblance to the embryonic enamel organ of the toothbuds. The resemblance is completed by the presence of stellate cells in the central parts of the cellular masses. The tumor is always the seat of an extensive degenerative

process. Perhaps the earliest change of the sort affects the central parts of the cellular masses and results in the appearance of stellate cells similar to those in the central parts of the enamel organ. But the process may go on to complete disintegration so that cystic spaces are formed, filled with a coagulum of albuminous material. In these cystic spaces gather also round globules which stain heavily with eosin, some of considerable size. Their nature is not known. Crystals of cholesterin are almost invariably present and many degenerated and desquamated cells. The connective tissue around the rare vascular channels becomes hyalinized and may also break down to form small cysts. Often also calcium salts are deposited in the hyalin and these deposits cast the characteristic spotty suprasellar shadow in the roentgenogram. Microscopically calcification is practically never absent but it is not always possible to demonstrate its presence with the roentgen rays. Often there are areas in which the epithelial cells have become cornified. The nuclei of these cells have degenerated and the cellular boundaries are indistinct, but it is possible to demonstrate them clearly when the cells are stained for keratohyalin; the cellular boundaries then appear as clear lines. The keratohyalin appears as granules which gradually coalesce in the cornified cells.

Near the base of the tumor the hypophysis will usually be found very much flattened, but with its characteristic granular cells still visible. The line of separation of the tumor from the brain is not always sharp, and projections of the tumor may extend like fingers some distance into the hypothalamic tissue. There is often a pseudocapsule of gliosis, but never a true capsule of connective tissue. One may find also isolated islands of epithelial cells in the region of the infundibulum which will give a clue to the ORIGIN OF THE CRANIOPHARYNGIOMA, now fairly definitely established.

If the region of the hypophysial stalk be examined in a number of normal individuals small masses of squamous epithelial cells will be found in the infundibulum or in the upper part of the hypophysis (20) but much more frequently along the anterior border of the stalk, especially at its superior and inferior extremities. The cells near the border of these groups usually resemble the basal cells of the epidermis, but within they may be clearer, larger, with typical intercellular bridges. There is generally no capsule of connective tissue. The masses may have a gradual transition into the columns of hypophysial cells, and chromophobe cells are occasionally found in the center of the groups

of squamous cells. Keratohyalin, horn, sweat-glands, sebaceous glands, and hair-follicles have never been found in these isolated rests.

Such groups of cells come into these regions in the following manner. In the very young embryo before the oral plate is open, while the epithelium of the stomodeum is still a single layer of cylindrical cells, an out-pocketing from the buccal cavity extends upward to meet the downgrowth of the infundibulum, in the manner we have already described (page 95), to form the hypophysis. In the third month of intrauterine life, the connection of this out-pocketing (which is usually known as Rathke's pouch) with the buccal cavity begins to disappear and is finally completely severed by the developing sphenoidal bone. In its further development part of the epithelium of Rathke's pouch follows for a certain time the same evolution as the epithelium of the stomodeum, becoming first cuboidal, then transitional, and finally squamous. But from the tenth week of fetal life there begins in the ventral part of the pouch a tremendous proliferation of cells, so that the original anterior wall of the pouch comes to lie on the anterosuperior part of the anterior lobe of the hypophysis and finally is pushed into the neighborhood of the stalk which it partially surrounds. It is in this region that remnants persist as nests of squamous epithelial cells from which doubtless the craniopharyngiomas arise.

SYMPTOMS from tumor of the craniopharyngeal duct may begin at almost any age, but usually under the age of fifteen. It is also interesting to note that the complaints of the patients vary according to their ages (64). Children complain of headache and vomiting and are found often to have choked discs. Failing libido, amenorrhea, and obesity are prominent among the complaints of young adults. Still older patients complain first of failing vision and headache. The adults rarely have choked discs; the incidence of intracranial tension is much higher in children. Any disturbance in the sexual sphere or in personal appearance is anxiously noticed at once by young adults; on the contrary with advancing age such alterations are accepted with more equanimity, and more or less as a matter of course, so that failing vision and headache usually first drive the patients to consult a physician. Yet a certain gamut of symptoms and signs runs through the entire group, different ones more prominent at different ages, even though it is very difficult to determine in many cases the exact chronological order of development of the insidious symptoms. I will describe them as they usually occur at various ages.

✓ Children are presented to the physician because of headaches and vomiting. There is nothing peculiar about the headache; ordinarily it is impossible to obtain from the little patient any very precise description. The vomiting is sudden and violent and occurs at most any time but especially on arising in the morning. This may be all that one can obtain from the patient or parents but occasionally there will be a complaint of persistent bed-wetting or that the child is delicate or too stout.

The first sign apparent to the examining physician is underdevelopment. The stunting of growth is practically constant but varies in degree. It is particularly striking when there is a fairly regular series of children in the family. Moreover the head is usually large for the size of the child. If it be percussed the cracked-pot sound, indicative of separated cranial sutures, will be elicited. The general habitus varies. One variant, known as the Lorain type, is delicate and slender; the skin is very thin and hairless; the whole impression is one of fragility. Another, called the Froehlich type, is rotund and sleek. In advanced cases an extreme emaciation develops; the child is irritable and often somnolent. Closer examination often reveals bilateral choked discs and bitemporal hemianopia, although precise visual fields are difficult to obtain from children. Very often a polyuria will be found to explain the bed-wetting; it is rarely extreme. The temperature may be very irregular, with often a low fever. There may be attacks of retraction of the head, accompanied by extensor spasm of the extremities, stupor, and vomiting. There is often a squint from palsy of the sixth nerve. A roentgenogram of the head will show that the cranial sutures are separated. The sella turcica is usually widened and appears shallow from erosion of the clinoid processes; in rare cases the sella may appear normal. But most important of all, usually above, but occasionally within the sella, is a patchy, spotty, or blotchy calcification characteristic of the tumors of the hypophyseal stalk.

Young adult patients may also come to the physician complaining of headaches or of failing vision but often of a series of troubles naturally absent in the children, namely, disturbances in the sexual sphere. If a young woman, it will be found usually that she is unmarried. The menses in these cases are tardy in appearing, perhaps have never appeared or have recently ceased. The breasts are undeveloped; the pubic and axillary hair scanty. The skin is delicate, hairless, and of a pasty color. The patient is often undersized and the contour of the body is childish so that one thinks again of infantilism. She is usually fat; has

always been so or recently gained rapidly in weight, but may be not only not fat but have a strangely wrinkled skin and aged expression which, combined with the small size, gives the impression of a little old woman. The young men are very similar except that their complaint is lack of libido. The genitalia are apt to be underdeveloped. If married they are often sterile. The bodily hair has a feminine distribution and the beard is scanty.

In these patients it is possible to examine more carefully the eyes. The most common defect in the visual fields is a bitemporal one, but if incomplete it rarely shows the typical topography and progression found with the pituitary adenoma. Bizarre alterations of the visual fields are common, such as central scotomas, lateral homonymous defects, inferior temporal defects, or irregular islands of vision. The central scotomas are probably to be explained by the fact that the craniopharyngiomas lie often back of the chiasm where they press early on the crossed macular fibers in its posterior border. These changes are accompanied by primary optic atrophy; choked discs are rare after childhood. The visual changes are usually preceded by headache which is described as being frontal, between or behind the eyes, less often bitemporal. It is sometimes accompanied by vomiting. These patients are often sleepy and have vague attacks of faintness accompanied by an unpleasant taste or odor but rarely by loss of consciousness or convulsions. The basal metabolic rate is low, sometimes as much as -35 or more, and the temperature is often subnormal. Polyuria and polydipsia are common. The bloodpressure is often low and the pulse rate slow. The x-rays reveal the same calcification in the region of the sella and the same erosions as in the children. There is, however, no dilatation of the cranial sutures.

✓ Toward middle life the patients seem particularly disposed to be thin and asthenic. Their skins, especially of the face, are covered by a myriad of wrinkles. Their bodily hair is usually reduced. They are usually of normal stature and the genitalia normally developed.

✓ The elderly patients come complaining of headache or of visual disturbances. Questioning usually elicits a history of increase in weight which may later have been lost, diminution of libido, impotence, or amenorrhea which precede by months or years the onset of headache. But these symptoms are often attributed to advancing age, ill health, or menopause and little attention paid to them. These elderly patients are rarely undersized and it sometimes requires close scrutiny to detect

alterations in bodily configuration, texture of skin, distribution of hair, and the other general changes so common in younger patients. The typical defect of the visual fields plus the findings in the roentgenogram make the diagnosis.

We must note now some uncommon symptoms of unusual physiological interest. Many patients have attacks of flushing and transitory edema or urticaria, giving evidence of a marked vasomotor instability. Sudden and unexplained febrile attacks are not uncommon. Children are usually placid or even cheerful; adults are usually even-tempered and sometimes indifferent to such an extent as to make one think of dementia praecox. In advanced cases there may appear ataxia and equilibratory disturbances, parkinsonian rigidity and bradykinesia (70), paresthesias in the back or extremities, spasticity of the lower extremities, attacks of extensor spasm of the extremities, paralysis of the third, fourth, fifth and sixth nerves or anosmia.

From our study of the morbid anatomy of these tumors we might expect symptoms from three sources: (1) intracranial hypertension, (2) disturbance of hypophysial function, and (3) compression of the neighboring nervous structures.

It is easy to understand that a tumor which occupies the region of the third ventricle should interfere with the circulation of the cerebrospinal fluid and so cause increased intracranial tension with its usual train of symptoms — headache, vomiting, swelling of the optic discs, slowing of the pulse — but it is not apparent why these symptoms do not often occur in adults in whom the tumor seems to reach a size equal to those of children. It is also evident that the resulting hydrocephalus will, in children, cause dilatation of the cranial sutures and increase in the size of the head.

The results of disturbance of hypophysial function I have already discussed. They are stunting of growth, infantile habitus, dearth of bodily hair, disturbance of sexual function, wrinkling of the skin, lowering of metabolism with its attendant lassitude and fatigue. We need not return to this subject (See page 108).

Compression of the neighboring optic chiasm is clearly the cause of the optic atrophy and of the defects in the visual fields. Theoretically we might expect a difference in the visual fields depending upon the origin of the tumor above or below the diaphragma sellae or upon the position of the chiasm before or behind the tumor (372). When the tumor lies above the chiasm one might expect a lower defect in the

visual fields and this is sometimes found but there seems to be no general rule in this regard. Usually when the patient comes first under observation there is a more or less complete bitemporal hemianopia. Homonymous defects are rare. The diplopia can occasionally be explained by a paresis of the sixth nerve, especially when there is intracranial hypertension, but often one must invoke in explanation the defect in macular vision which makes binocular vision possible only by the use of heteronymous fields (115). Occasionally late in the course of such a tumor it may reach such size as to compress the third, fourth, or sixth nerves in the wall of the cavernous sinus and so cause diplopia; such cases are rare.

In order to understand the other neighborhood-symptoms we must make an excursion into the STRUCTURE AND FUNCTION OF THE HYPOTHALAMUS, a region of the brain which is too briefly dismissed in your manuals of anatomy and physiology. The *topography of the hypothalamic region* is portrayed in Figures 53 and 54. It lies just above the hypophysis cerebri and is connected with the pars nervosa by a narrow stalk of nervous tissue surrounded and permeated by many bloodvessels. Between the two hypothalami is the narrow downward extension of the third ventricle known as the infundibulum. The nervous tissue forms a funnel, when regarded from the outside, called the tuber cinereum. Anteriorly lies the optic chiasm, and the hypothalamus extends a variable distance in front of it, as far as the anterior perforated space, in a narrow zone known as the supra-optic lamella. The optic tracts clasp the hypothalamus like two arms on either side. The mamillary bodies mark the posterior boundary. On the inner wall of the hypothalamus, the columns of the fornix may be seen to pass diagonally from the anterosuperior angle to the postero-inferior. Anteriorly the hypothalamus is separated by the lamina terminalis from the telencephalon; superiorly a groove marks its junction with the epithalamus; posteriorly it passes without definite delimitation into the tegmentum of the mid-brain.

Within the hypothalamus a number of *nuclei* have been distinguished (330). Throughout the hypothalamus are scattered very small cells practically without cytoplasm; their nervous nature is betrayed by their vesicular nuclei. They form the *substantia grisea centralis*. These small cells seem to form a substratum of relatively underdeveloped nervous cells out of which certain groups are differentiated into more or less definite nuclei. The most ancient seems to be the nucleus supra-opticus

which curves in the form of a crescent over the optic chiasm. Its cells also follow the optic tracts for a short distance lateroposteriorly. They are fairly large and their tigroid substance is grouped in the periphery of the cytoplasm. They are closely clustered into a compact mass. The nucleus paraventricularis is an oval discrete mass of cells lying close to the ventricular surface, medial to the column of the fornix. It stretches between the chiasm and the massa intermedia. Its cells are somewhat smaller than those of the nucleus supra-opticus and their nuclei are larger. The tigroid masses, although massed in the periphery of the cytoplasm are smaller and stain less intensely. The cells of the nucleus tuberomammillaris are diffusely scattered from the nucleus supra-opticus to the mammillary body which they surround on its ventral and dorsal sides. They surround also the columns of the fornix. The tigroid substance of these cells is more diffusely distributed through the cytoplasm. They are of moderate size. The nuclei ruberis laterales consist of several nests of small cells on the periphery of the tuber cinereum. Their cells are compactly arranged and differ sharply in structure from those of the surrounding nuclei; they contain very little tigroid substance but are filled with yellow pigment. These nuclei seem to be phylogenetically young. They are difficult to identify in some monkeys and their identity in lower mammals is disputed. Extending back above the corpus mammillare toward the tegmentum mesencephali are the large cells of the nucleus reticularis hypothalami. They have large discrete tigroid masses characteristic of motor cells.

The interrelations of these various nuclei (except the mammillary bodies and corpus subthalamicum) are very imperfectly known. They are supposed by physiologists to constitute a sort of head-ganglion for the sympathetic nervous system. It is interesting, therefore, to note that their cells do resemble very closely the sympathetic cells of the intermediolateral columns of the spinal cord. It is also interesting that only the cells of the nucleus intercalatus of the mammillary body and of the nucleus reticularis hypothalami have the large discrete tigroid masses characteristic of motor cells. It is known that from the nucleus reticularis hypothalami fibers extend backward into the tegmentum mesencephali (tractus reticularis hypothalami). Descending fibers from the cells of the nucleus tuberomammillaris are thought to do likewise. How far these fibers go is not known but, judging from the structure of the cells, only those of the nucleus reticularis are clearly motor. The cells of the nucleus tuberomammillaris, nucleus paraventricularis, and nucleus

supra-opticus have the characteristic structure of intercalated neurones. The nucleus supra-opticus sends fibers to the posterior lobe of the hypophysis cerebri (tractus supra-opticohypophyseus). From the nucleus paraventricularis a band of fibers streams toward the infundibulum (tractus paraventricularis cinereus); its termination is unknown. The nuclei tuberis laterales are unique in structure. They receive fibers from the frontal region (tractus frontotuberis) whose origin is undeter-

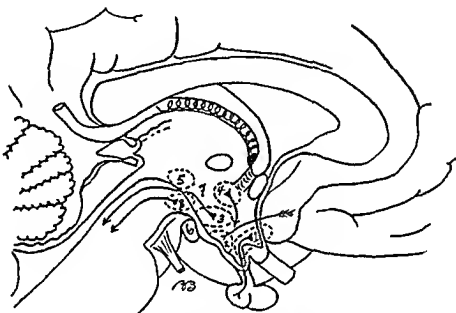


FIG. 53. Scheme of median surface of the hypothalamus to show nuclei and tracts. 1—supra-optic nucleus; 2—nuclei tuberis laterales; 3—nucleus rubro-mammillaris; 4—nucleus paraventricularis; 5—corpus subthalamicum; 6—corpus mammillare; 7—substantia grisea centralis; 8—substantia reticularis hypothalami.

mined; they are said to send backward toward the midbrain (tractus tuberis) fibers whose termination is likewise unknown. It is probable that the hypothalamic nuclei and their fibers belong to a relatively undifferentiated, phylogenetically old, part of the brain and that there are no clearly differentiated long fiber-systems but rather short chains of neurones. At any rate few inferences can be drawn from their structure and relations which will aid us in understanding the effects of lesions

of the hypothalamus. The most definitely established facts are summarized in Figure 53.

The hypothalamus is very small but lesions in this region of the brain cause unexpectedly numerous symptoms. These usually occur in combination but since they may occur isolatedly it has been supposed that each nucleus has a separate function. Isolated lesions of the individual nuclei may be produced by softenings because of peculiarities of the blood-supply of the hypothalamus. Its arteries penetrate into the tuber in vertical parallel series (Fig. 54). The anterior communicating artery sends small branches to the supra-optic lamella. From the anterior cerebral artery come long tortuous branches which run on the

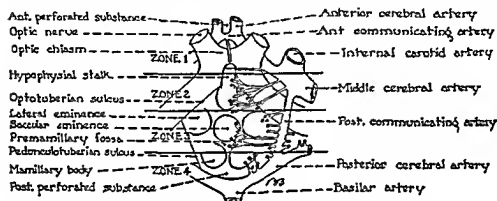


FIG. 54. Hypothalamus from below to show arterial supply (after Leblanc).

under surface of the chiasm to the infundibulum and stalk, and bundles of small arteries to the upper surfaces of the optic tracts and the optoperforate zone. The internal carotid artery gives off two branches, just before the communicating artery, which run on the under surface of the optic tract straight to the lateral and posterior parts of the pituitary stalk. The posterior communicating artery gives off two sets of branches—the superficial ones going to the lateral and saccular eminences and spreading anteriorly in the optotuberian sulcus and posteriorly in the premammillary sulcus, the deeper branches going to the deeper parts of the same region. Finally, sometimes from the posterior communicating artery sometimes from the posterior cerebral, an artery supplies the mammillary body and the prepeduncular fossa. The tuber cinereum may be divided thus into four zones: (1) the suprachiasmaic zone supplied by branches of the anterior communicating and the anterior cerebral arteries; (2) the pituitary stalk, and the region between

ir and the optic tract, supplied by branches of the internal carotid artery; (3) the lateral and saccular eminences, and the optotuberian sulcus, supplied by branches of the posterior communicating artery; and (4) the mammillary bodies and prepeduncular fossa supplied either by the posterior communicating or posterior cerebral arteries. The supra-optic nucleus is supplied by the branches from the anterior cerebral artery, the nuclei tuberis laterales and tuberomammillares by branches of the internal carotid and posterior communicating arteries of zones 2, 3, and 4. The nucleus paraventricularis is supplied by long branches from the posterior communicating artery which run beneath the ventricular epithelium. The larger branches of these arteries penetrate in the fissures. The mammillary bodies and the nucleus reticularis hypothalami are supplied from the posterior cerebral or posterior communicating arteries. It is possible, therefore, to have softenings from vascular occlusion which would be restricted fairly well to a single nucleus.

From the study of such lesions and others in this region it has been concluded that the paraventricular nucleus has a special relation to the metabolism of carbohydrates, the supra-optic nucleus to the metabolism of water and the nuclei tuberis to the regulation of heat. There is at present, however, no general consensus and the problem, although very important to physiologists, has little importance for the study of brain-tumors which make, usually, gross lesions of the nervous tissues. *Physiological experimentation* has confirmed the significance of the hypothalamus as a whole (53). *It seems fairly clear that this region is an integral part of the mechanism which controls reactions in the sphere of the sympathetic nervous system.* When one remembers how diffuse is the structure of the sympathetic nervous system, that there are few definite bundles of fibers in the hypothalamus, that physiologically the sympathetic system reacts largely as a unit, and that in the clinic all the various symptoms are usually associated, it seems improbable that any attempt to assign specific functions to the various nuclei should succeed. Under these circumstances I feel it best at present to discuss the functions of the hypothalamus as a whole.

If in a cat the central nervous system anterior to the hypothalamus, including the basal ganglia and most of the thalamus, is removed the animal still is able to regulate its temperature, but enters after half an hour or so into periodic attacks of a peculiar nature (54). He thrashes about, strikes out with his paws, extrudes the claws, snarls and spits.

lashes the tail, and pants vigorously with the mouth open. At the same time there is sweating from the toe-pads, rise in bloodpressure, acceleration of the heartrate, erection of the hairs on the tail, retraction of the nictitating membranes, exophthalmous, and dilatation of pupils. The animal in other words gives evidence of being in a violent rage, accompanied by the usual diffuse results of a sympathetic discharge. When the hypothalamus is now removed by section passing from the anterior colliculi, just back of the mammillary bodies, these attacks disappear and the animal can no longer regulate its temperature. If the section is made primarily at the latter level the attacks of rage do not appear. Moreover, it has recently been shown that if the frontal region in the cat be separated from the hypothalamus by a transverse cut anterior to the optic chiasm the animal is transformed from a docile friendly creature into a snarling vicious beast (222).

If we take another cat and stimulate the hypothalamus electrically, widespread physiological reactions are obtained. By stimulation lateral to the infundibulum one obtains widening of the pupil, narrowing of the palpebral fissure, and retraction of the nictitating membrane. General vasoconstriction, sweating, secretion of tears, contraction of the pregnant uterus and of the intestine, have all been reported to follow stimulation either of the hypothalamus or subthalamus. Similar results are obtained in other animals. For example, in the pigeon several weeks after decerebration, if the deep ventricular surfaces of the diencephalon posteriorly be stimulated electrically, there occur movements of the eyes and constriction of the pupils followed by sudden flying and circular movements (410). Sometimes there is obtained an elevation of the temperature of the body with erection of the feathers, shivering, and muscular tremor. The temperature-reaction may be obtained much more easily by cooling the region with a piece of ice. In addition it should be noted that a marked diuresis follows in the twenty-four hours following stimulation (411).

If the hypothalamus be acutely injured a new train of phenomena appears. One of the most striking results is an intense polyuria (40). A dog which has been punctured in this region may pass as much as five liters of urine in a day. The polyuria is preceded by polydipsia and is usually most intense in the days immediately following the injury, but may last for weeks and months. The same effect has been obtained in the cat (193) and the rat may be caused to drink twice its body-weight in the course of a day. The decerebrate pigeon may dehydrate itself and

die. Another frequent symptom is glycosuria. Ordinarily the glycosuria occurs only in the first twenty-four hours, but by introducing into the hypothalamus of a rabbit a small glass-tube filled with fatty acids, there has been produced a glycosuria which appears generally about the fifteenth day, reaches as much as 65 grams per liter of urine, and lasts from nine to as much as fifty-five days. After a long period of latency a marked adiposity may result. This has been observed in the dog and rat (448). Such a rat is shown in Figure 43 compared with a littermate and with another rat of the same age from which the hypophysis has been removed. The deposition of fat is general in the dog, the visceral organs as well as the subcutaneous tissue being involved. It is important to note that this adiposity is associated with a marked atrophy of the genitalia. Recently it has been shown also that the hypothalamus is related in some way to the heart. Under chloroform-anesthesia stimulation of the posterior portion of the hypothalamus produces an extrasystolic cardiac arrhythmia. This arrhythmia can no longer be elicited after the hypothalamus has been severed from the midbrain or after a destructive lesion of its posterior portion.

Immediately following a destructive lesion of the hypothalamus there is frequently a sharp rise in temperature. If the animal survives, its temperature subsequently becomes subnormal. Such animals huddle against radiators and steam-pipes and the hair is not erected even in the coldest weather. It has been abundantly proven (396) that sympathetic centers in the hypothalamus are in control of the bodily temperature.

It has been noted that animals after injury to the hypothalamus are particularly somnolent. It is known that decorticate dogs sleep (301) and that cats from which cortex and striatum have been removed will sleep. Sleep has been produced in cats by electrical stimulation of the region around the anterior end of the aqueduct of Sylvius; to produce this effect an optimal current is necessary, stronger stimulus awakening the animal. Injection of small amounts of calcium chloride into the central gray matter in the region of the infundibulum in cats produces sleep, characterized by slowing of the pulse and respiration, narrowing of the pupil and appearance of the nictitating membrane. Injections into the surrounding regions never cause sleep.

All of these symptoms which have been obtained in experimental animals may be duplicated by the effects of lesions of the human hypothalamus (220). In fact most of the experiments were undertaken in

the search for an explanation of pathological conditions in man. As early as 1890 it was pointed out that a disease in which the pathological lesion predominated in the gray matter around the aqueduct of Sylvius was associated with an exaggerated sleepiness. When in 1917 there was a recrudescence of this disease it was given the name of lethargic encephalitis (Economo's disease). It caused in the course of the epidemic nearly all the symptoms which we have enumerated above and a multitude of others. Not the least amazing of these were the perversions of sleep, not only somnolence, but inversion of the sleep-rhythm. There are records of other nonexpansive lesions in the hypothalamic region associated with pathological sleepiness, such as embolic abscess or thrombosis. Of course any intracranial tumor when it has produced a sufficient degree of intracranial hypertension may cause stupor, but the drowsiness which occurs in the absence of any signs of intracranial hypertension is always associated with a tumor in the region of the third ventricle, such as the tumors of the hypophysial duct.

With the polyuria produced in animals corresponds a disease known in man as diabetes insipidus, in which the patient passes tremendous quantities of a very dilute urine. This disease has been produced in man by gunshot wounds of the hypothalamus, by leutic endarteritis, by epidemic encephalitis and by destructive nonexpansive tumors. Diabetes insipidus may occur as an isolated disease but is often associated with adiposity and genital dystrophy, and also with hypersomnia. There has long been an argument concerning the relationship of the posterior lobe of the hypophysis to these symptoms; there can be no question that all these symptoms may arise from lesions of the hypothalamus which leave the hypophysis intact.

Tumors in this region are peculiarly liable to be accompanied by fever so that a diagnosis of encephalitis is frequently made (459), and it has long been known that operations in the region of the third ventricle are particularly hazardous because of the frequency of a postoperative hyperthermia which is almost invariable, and may be uncontrollable so that the patient dies with a temperature of 43° or more. During the period of hyperthermia the patient is semiconscious or quite unconscious, the pupils are contracted, sweating is absent, and cardiac irregularities may appear. If the acute disturbance improves there may appear a diabetes insipidus, even in cases in which it had been absent before operation. The temperature now becomes subnormal and the patient may develop a cachectic state from which he dies.

Some interesting observations have been made during operations in this region under local anesthesia. Maniacal attacks have been provoked in which flight of ideas went even to incoherence (Foerster) and was associated with disorientation. Sleepiness has also been produced; a child who a moment before was talking with the surgeon (Vincent) suddenly went to sleep. When awakened a few moments later he said, "Let me alone. I want to sleep. I am sleepy." He had, therefore, a feeling of sleepiness. For the next four or five days he continued to sleep and when aroused to eat repeated "Let me alone. I am sleepy." It is not uncommon after operations in this region under general anesthesia to have the patients exceedingly somnolent for many days. Occasionally manic excitement develops. Here is a typical example of the sort of postoperative reaction one may obtain (33); A boy of thirteen from whom a tumor of the third ventricle had been removed made an excellent recovery from his anesthetic. The wound healed perfectly and the patient's pulse and respiration continued good but he developed a most remarkable reaction. He was very restless, rolling and tossing constantly, crying and whining incessantly. He would answer only after persistent questioning but his answers indicated perfect comprehension. This state of affairs persisted for nearly two weeks at the end of which time he still preferred to stay in bed curled up, with his head under the covers, complaining that he was cold. He would answer questions but always ended by weeping. The involuntary movements of his limbs made it impossible for him to walk. There was little spasticity but definite resistance to passive motion. Definite coarse tremor of both hands was present. His speech was jerky, but there was no definite dysarthria and no dysphagia. He was troubled very much by insomnia, scarcely sleeping at all, and weeping or laughing on any stimulation. The symptoms gradually disappeared until by the end of the third week he was normal again. It was impossible during this time to make a careful examination because of his extreme restlessness. His temperature remained above normal until the nineteenth day.

Such observations as these have made us believe that *the basal regions of the brain must exert a regulatory influence upon the cortex cerebri* (98). The nuclei and tracts involved are unknown but two mechanisms are invoked, one situated anteriorly in the anterior inferior part of the central gray matter around the third ventricle which excites, and another around the posterior superior part of the third ventricle and aqueduct of Sylvius which calms and quiets. The symptoms of the latter

region are fatigue, sleepiness, stupor, slowing of thinking, and dimming of consciousness. At any rate it is proved that the hypothalamus is intimately associated with the sympathetic nervous system and with the expression of emotion. That the last two are inseparable has been amply demonstrated (101).

In view of the foregoing evidence there can be little doubt that, of the symptoms which patients with craniopharyngioma develop, the following reveal a disturbance of the nervous structure of the hypothalamus or the adjacent regions of the midbrain: polyuria, adiposity, hypersomnia, hyperthermia or hypothermia, cardiac irregularities, emotional disorders, and in part perhaps the genital dystrophy; these include the two well-known clinical syndromes of diabetes insipidus and adiposogenital dystrophy. Rarely pubertas praecox seems to be produced by a lesion in this region (275).

Other rare symptoms which we have noted above may be variously explained—the spontaneous pains by compression of the epithalamus, the bradykinesia and rigidity by compression of the extrapyramidal motor pathways, the ataxia by involvement of the red nuclei or superior cerebellar peduncles or frontopontine tracts, the mental deterioration by chronic hydrocephalus, the pseudobulbar phenomena by pressure on the corticobulbar pathways.

★ **DIFFERENTIAL DIAGNOSIS** must be made largely from the adenomas of the hypophysis. The age of the patient is of some assistance, since adenomas almost invariably develop after the age of fifteen (Fig. 47). The roentgenogram of the sella turcica is also helpful; the sella is enlarged by an adenoma almost always in symmetrical fashion, while by a tumor of the hypophysial duct the sella as a rule is widened and flattened and the clinoid processes eroded. The suprasellar calcification of the craniopharyngioma is very rarely found with an adenoma. The clinical symptoms are also different; the adenoma is never accompanied by a polyuria and rarely by stunting of growth, whereas acromegalic symptoms, at once make a diagnosis of adenoma. The visual fields in cases of adenoma are usually regular and any bizarre visual defects should make one think of a craniopharyngioma. Central scotomas are much more frequent with craniopharyngiomas although rarely a rapidly developing adenoma will cause such a defect. Patients with either lesion are apt to be inactive but the one with an adenoma complains of fatigue and lassitude; the other more often of sleepiness. The headache is of the same character in both and papilledema, occurring only in children

(with rare exceptions), is seldom of any aid. Tumors of the hypophysial duct seem to be able to reach a greater size before causing serious visual disturbances; perhaps for this reason one sees a series of symptoms rarely associated with adenomas, such as ataxia, bradykinesia, pains in the body, and extremities (found also in acromegaly from a different cause), tonic extensor spasms, spasticity and transitory edemas.

In children these tumors must be differentiated from the midline cerebellar neoplasms. In typical cases the diagnosis is easy but sometimes their differentiation is exceedingly difficult. There is a dearth of cerebellar symptoms in many cases of midline cerebellar tumors. Moreover, the internal hydrocephalus caused by tumors in the cerebellar fossa affects also the infundibulum of the third ventricle which presses downward into the sella turcica, enlarging and eroding it (132). The hypophysis, moreover, is compressed as well as the hypothalamus, causing stunting of growth. When one remembers that the tumor of the

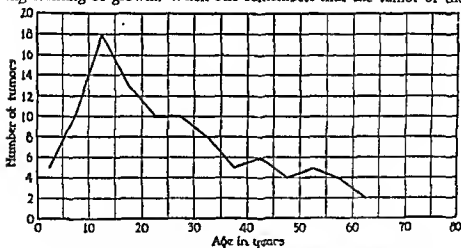


FIG. 55. Graph of age-distribution of craniopharyngiomas.

✓ hypophysial duct may give rise to definite cerebellar symptoms (32), high intracranial tension, separation of the cranial sutures, and that a suprasellar calcification may be absent, the difficulties of the situation may be appreciated.

There is another tumor of childhood with which the craniopharyngioma may be confused—the glioma of the optic chiasm. One may suspect such a glioma if the child has peripheral manifestations of generalized neurofibromatosis. It may be positively identified by the demonstration of dilatation of the optic foramina. In all children whose symptoms in-

dicare an involvement of the hypothalamic region, and in whom no suprasellar calcification can be demonstrated, it is wise to make roentgenograms of the optic canals. These children may have polyuria, adiposity, and many other general symptoms of tumors of the hypophyseal duct, but rarely the typical arrest of growth.

Chronic circumscribed arachnoiditis (112) may sometimes simulate these tumors but there is, of course, no suprasellar calcification in these cases, and the sella itself is normal. Signs of involvement of the hypophysis or hypothalamus are usually absent. At the onset of symptoms the visual acuity is rapidly lost without visible change of the fundus. Central scotomas are frequent and early; bitemporal hemianopia is rare.

In the adult must be differentiated also the meningioma developing from the tuberculum sellae (143). The diagnosis is made difficult because both the adenoma and the craniopharyngioma are likely with advancing age to give fewer and less-striking general constitutional symptoms so that, in all three, the symptoms may be largely confined to alterations in the visual fields. Although in a patient beyond middle age the gradual development of a bitemporal hemianopia without other symptoms means usually a meningioma, a positive diagnosis cannot always be made without biopsy.

Mistakes may be made with rarer tumors of the third ventricle also. The positive identification of a tumor of the hypophyseal duct before operation rests largely on the suprasellar calcification, which is present in 85 percent of the cases (335) and when typically developed is almost pathognomonic.

The only logical TREATMENT is to remove the tumor, but it lies in a very inaccessible situation in the center of the brain. Guarded in front by the optic chiasm, on the sides by the carotid arteries, behind by the brainstem, surrounded by the circulus arteriosus, it seems to defy the surgeon. Luckily it is attached, and receives its blood-supply, largely at the base. Its upper part is usually cystic. After the cyst is emptied the wall can often be pulled out without provoking any hemorrhage; it is not sufficient simply to puncture the cyst because it soon refills. But if the cyst is of considerable size the results of the collapse of the basal regions of the brain, as we have already remarked, may be disastrous. And if the diencephalon should manage to recover its equilibrium we have no means of relieving the hypophyseal deficiency. There is no other hope in these cases, but the mortality and morbidity from operation will doubtless continue to be very high.

CHAPTER 7

TUMORS OF THE INTRACRANIAL CONNECTIVE TISSUES

GENERAL DISCUSSION

SARCOMA

MELANOBLASTOMA

Whereas in the earlier statistics concerning intracranial tumors sarcomas constituted some 40 percent of the total (455), in more recent statistics they are often not even listed. This can mean only that the use of the term has changed. In the former sense of a rapidly growing cellular fleshy tumor, sarcomas are still quite common. But in the modern sense of malignant tumors of mesodermal origin they are rare in the intracranial cavity. Yet there are occasionally tumors for which the word is still proper and among them a diffuse neoplasm often called SARCOMATOSIS OF THE MENINGES. Here is the brain of such a case (Fig. 56). Its gross appearance is that of tuberculous meningitis. In fact such was the diagnosis made by the pathologist at necropsy and rectified only after microscopical study.

The patient (CASE IX) from whom this brain was taken was a woman of forty-five years who, according to her husband, had had headaches, diagnosed as migraine, all her life. There was also a familial history of migraine. At the age of thirty-three, following the birth of the second of her two children, she suffered from a "nervous breakdown," characterized by "weakness, nervousness and being tired." This lasted for three years, during which time the patient complained of frequent attacks of pain and stiffness of the neck. For the last four months of her illness this pain and stiffness had been more severe and constant. She tended to keep her head bent forward. Her husband noted that she was becoming increasingly irritable. One month before admission to the hospital she developed numbness of the right side of her face and neck and of her right hand. It was frequently observed that she could not feel light objects, such as a handkerchief, with her right hand. About this same time she began vomiting profusely and continuously. She had visual hallucinations and saw objects such as flowers, farming machinery, and people. She also developed an inward rotation of the right eye and complained of diplopia. This soon disappeared, only for the left eye to become similarly involved soon afterward. It was also observed that

her respirations were frequently deep and sighing. During the last week she was irritable. The last four months of her illness had been characterized by frequent relapses and remissions.

The patient was found on admission to be very restless. There were constant purposeless movements of her extremities, especially of the arms. At times she seemed to make an effort to speak, but only un-

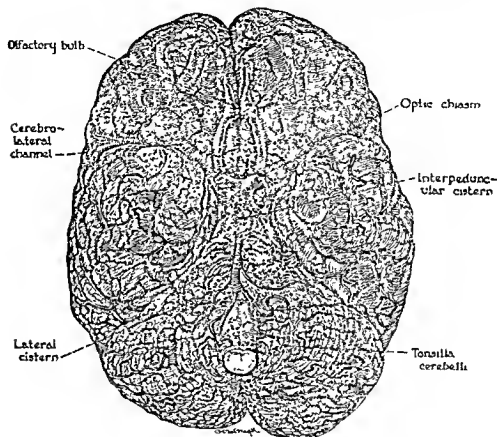


FIG. 56. Brain of CASE IX. Thickening of the leptomeninx resembling tuberculous meningitis

intelligible sounds resulted. Her respirations were deep and sighing, sixteen to eighteen per minute. The temperature was normal, pulse 70 to 80, and bloodpressure 170/92. Her neck was very stiff and there was a bilateral Kernig's sign. There was a right facial weakness and a palsy of the left external rectus muscle. The optic discs were normal. All other cranial nerves seemed normal. The extremities seemed strong; there was no evident paresis. The reflexes, both cutaneous and deep, were

generally diminished but equal on the two sides. There seemed to be a definite diminution in response to pin-prick on the right side of the body as compared with the left. Spinal fluid had been obtained by lumbar puncture at another hospital and was reported to be normal. She had a leucocyte-count of 15,000. The roentgenograms of the skull were not very satisfactory, but those obtained appeared normal.

A positive diagnosis was impossible but it was thought that the patient might be suffering either from a tumor in the cerebellar fossa or from an encephalitis. It was decided to make a ventriculogram the following morning, but she died in the course of the evening. The death was definitely due to respiratory failure; the heart continued to beat long after respiration had ceased.

Permission was obtained for examination of the brain. This was made three hours postmortem. There is, as you see, no gross evidence of tumor of the brain. The convolutions are somewhat flattened and hyperemic. The ventricles are slightly dilated. The leptomeninges are cloudy and thickened, especially around the base of the brain. A diagnosis of tuberculous meningitis was made from gross examination of the brain, but microscopical examination proved this diagnosis to be erroneous. The leptomeninges practically everywhere is actually transformed into a diffuse tumor which extends to the depths of the sulci and even accompanies the bloodvessels for several millimeters into the cortex. The deeper vessels are not seen to be involved.

The neoplastic cells lie in an abundant network of reticulin. Collagen is found only around the larger bloodvessels. Many of the cells, especially near the vessels, resemble lymphocytes; they have small, round, heavily stained nuclei and very little cytoplasm. Other cells are elongated, but most numerous are polygonal or rounded cells with abundant eosinophilic cytoplasm and eccentrically situated nuclei (Fig. 57). Many of the latter resemble signet-rings. Mitoses are frequent. There is no melanin in the cells. The tumor extends to the tip of the bulb, very probably also to the leptomeninges of the spinal cord which, unfortunately, we were not permitted to examine. In similar cases the spinal meninges have been found also to be transformed into tumor (60); here is an example of such an extension.

A young girl (CASE X) of nineteen years awoke nauseated and vomiting one night about three months before her admission to the hospital. Previously she had been well except for a peritonsillar abscess two years before, and was counselor at a girl's camp at the time of her ill-

ness. About one week later another period of nausea and vomiting kept her in bed all day. Since that time she remained in bed. Whenever she attempted to get up she had a severe headache and vomited. She soon began to complain of double vision, and the left side of her mouth drooped.

When admitted she preferred to lie on her right side, saying that in this position she was less dizzy and nauseated. It made her head

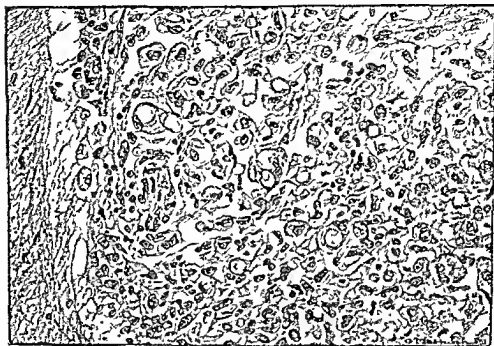


FIG. 57. Drawing of microscopical preparation of meningeal sarcoma from CASE IX. Surface of cerebrum at left.

ache to flex it anteriorly. It was difficult for her to move the eyes conjugately to the right; conjugate movements upward and to the left were normal. There was no definite nystagmus, at most a few jerks when looking to the extreme left. She was unable to converge. There was a slight hyperemia of the optic discs but no measurable elevation. The pupils reacted normally to light. More careful investigation of the diplopia seemed to indicate a weakness of the left internal tectus muscle. There was a peripheral paresis of the left facial nerve and some diminution of sensory acuity over the left side of the face. No disturbances were found in the upper extremities. The lower extremities were normal ex-

cept that the left ankle-jerk was brisker and there was a questionable left extensor plantar reflex. There were no symptoms of involvement of the cerebellum.

The most definite findings were the left facial palsy and disturbance of conjugate movements of the eyes. With acuity of the left ear normal (caloric tests were not made because of the patient's condition) a tumor in the left cerebellopontine angle seemed unlikely. There was no indication that the cerebellum was primarily involved. The fact that there was only slight swelling of the optic discs made it possible that the tumor lay within the pons but there seemed too few pyramidal and sensory symptoms to make this localization probable. It was finally decided that the tumor most probably lay in the fourth ventricle and a suboccipital exploration was made. There was disclosed a soft reddish-gray mass of tumor filling the posterior cistern and extending over the surface of the right cerebellar hemisphere down into the spinal canal and around the bulb into the right cerebellopontine angle. The tumor did not extend into the fourth ventricle. As much as possible of this tumor was removed. After operation the patient's respirations were very irregular, labored, and shallow. Her speech was indistinct. She gradually became comatose. It was thought that a hematoma must be forming so the wound was reopened. The cerebellum was very edematous and some clotted blood was removed. Although there seemed to be no compression of the bulb a laminectomy of the first and second cervical vertebrae was made. Her condition did not improve and she died a few hours later.

A complete examination was made, three hours postmortem, which disclosed a diffuse tumor spreading in the leptomeninges over the base of the brain (Fig. 58) as far forward as the olfactory region and down the spinal cord to the cauda equina. The tumor spreads upward between the frontal lobes and back over the corpus callosum. It completely surrounds the midbrain, being about 2 mm. thick over the corpora quadrigemina. It extends into the sheath around the left gasserian ganglion. Over the spinal cord the thickest infiltration is on the posterior surface. In the cauda equina are several rounded nodules about a centimeter in diameter among the roots.

It was long thought that meningeal tumors arose from the dura mater, hence the name *fungus duræ matris* formerly applied to them, but evidence of a leptomeningeal origin has accumulated since the study of M. B. Schmitt in 1902 to such an extent that it is now doubtful whether any tumors arise from the pachymeninges. The proper interpre-

tation of the peculiar structure and distribution of these tumors necessitates an intimate knowledge of the ORIGIN AND STRUCTURE OF THE MENINGES.

According to the classical description of embryologists the leptomeningx, as well as the pachymeningx, arises from the loose tissue of the cephalic region of the embryo, the mesenchyme of which condenses to form two layers, the primordia of the two membranes. A cleft appears

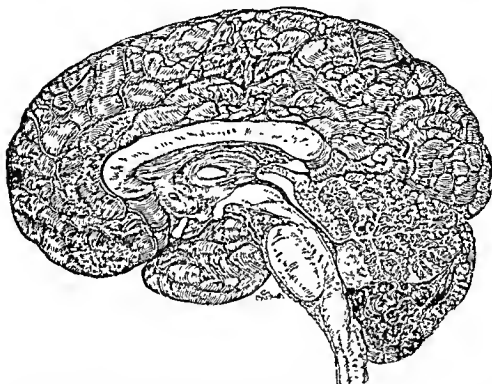


Fig. 58. Median section of brain from CASE X. Tumor (stippled) fills the basilar and interpeduncular cisterns and surrounds the midbrain; it has been removed from the posterior cistern.

between them to form the subdural space. Later a clear fluid appears in the spaces of the leptomeningx in the region of the fourth ventricle and gradually spreads, splitting this membrane incompletely into the arachnoid and pia mater and forming the subarachnoid space (502). We have already noted that the subdural space is merely potential, whereas the subarachnoid space is in some regions quite large and contains a considerable quantity of fluid. The two membranes, in this view, have a unique origin but their behavior (in the healing of wounds,

in the formation of tumors, etc.) is so different that it has often been urged that the classical description of their formation must be incorrect (246).

In the embryo of the chick the origin of the mesenchyme can be traced clearly from a proliferation of cells at the junction of entoderm and ectoderm along the primitive streak. This process is familiar to every medical student. Along the primitive streak also the ectoderm invaginates to form the neural tube. Then a second proliferation of cells occurs on each side at the junction of neural tube and ectoderm; it is called the neural crest. From it is formed the sympathetic nervous system, the neurilemma and the medulla of the adrenal gland, and in it has been sought the origin also of the leptomeninges. The experimental evidence has been disputed but there remains the otherwise inexplicable fact that meningeal tumors are often associated with tumors of the peripheral nerves in the pathological complex of generalized neurofibromatosis (von Recklinghausen's disease) (466). The peripheral tumors arise from the neurilemma which is formed by the neural crest; their association with meningeal tumors would be easily understandable if the leptomeninges were also of similar origin.

We may confine our attention to the structure of the leptomeninges since, whatever may prove to be its origin, there can be no doubt that *practically all meningeal tumors arise from it*. It is composed of cells resembling those of the connective tissues elsewhere in the body. Within the membrane they are elongated and form collagen, elastin, fibroglia, and reticulin; they should, therefore, be classified as fibroblasts. On the outer surface of the arachnoid next the subdural space, lining the subarachnoid space, and on the inner surface of the pia mater next the nervous tissue, they are flattened and resemble the cells lining the pleural or peritoneal cavities. In these situations they are better spoken of as mesothelial or perhaps meningotheelial cells. The cells of the pia mater next the nervous tissue are sometimes distinguished by the term *intima piae matris*. The subarachnoid space is traversed by bloodvessels. The latter are covered by leptomeningeal cells which they carry with them when they plunge into the brain. Near the surface, especially around the larger vessels, the two layers of the leptomeninges can be distinguished and also the subarachnoid space forming the so-called pial funnel (Fig. 59). Deeper within the brain there is only a meshwork of loose connective tissue forming the perivascular sheaths, in the meshes of which may be found a few lymphocytes and clasmatocytes (307). In

pathological processes this meshwork is infiltrated by lymphocytes, distended by hemorrhage or by edema to form the perivascular space (of Virchow-Robin). Around the smaller vessels one can find only a sheet of cytoplasm which contains rare elongated nuclei and winding fibrils of reticulin; it is called the *perithelium*. Around the capillaries the presence of a leptomeningeal sheath is disputed. But certainly one finds there scattered stellate adventitial cells (of Rouget). The leptomeninx therefore permeates the brain throughout.

The intima piae matrix is in close contact with the neuroglia. The neuroglial cells by means of their perivascular processes, which spread

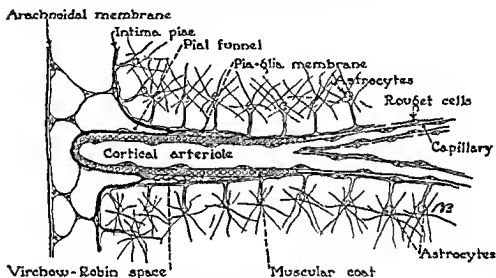


FIG. 59. Scheme of perivascular structures within the cerebral cortex.

out on the surface of the intima piae matrix, help to form between the connective tissue and the interstitial tissue of the brain a barrier which is known as the pia-glia membrane. It is, generally speaking, impermeable to cells coming from the bloodstream which may, however, circulate freely within the perivascular connective tissue. When the neuroglial cells die the connective tissue proliferates and a scar is formed. It is as if the pia-glia membrane normally held the connective tissue in check (425).

But the leptomeninx does not penetrate inward only. Along the venous sinuses it perforates the dura mater in numerous small nipples and so is bathed directly by the venous blood (Fig. 60). These arachnoidal granulations (of Pacchioni), as they are called, may penetrate

entirely through the dura mater and erode the bone. Through the openings they have made the brain may herniate in cases of increased intracranial tension (518). It is important to note that the arachnoidal granulations are composed largely of cells of the meningotheial type which form few or no intercellular substances. Along the surface of the arachnoidal membrane may often be found accumulations of such cells which have not penetrated into the dura mater. These cellular masses sometimes undergo hyaline degeneration, become calcified (145) and even

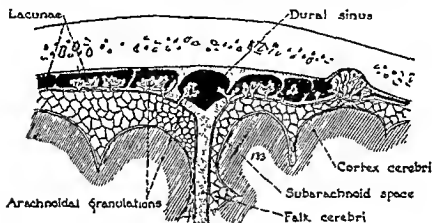


FIG 60. Drawing showing the relations of the arachnoidal granulations to the dural venous sinuses (after Key and Retzius).

true bone may form within them. The leptomeninx also accompanies the cranial nerves for a variable distance within their foramina of exit from the cranium, especially the optic nerve, which is really a part of the brain. The exact relationship of the leptomeningeal sheath to the neurilemmal sheaths of the nerves is disputed.

Wherever the leptomeninx extends it has the microscopical structure of connective tissue and this fact is reflected also in the structure of meningeal tumors which develop from it (43). Rarely such a tumor will be composed of the loose stellate and fusiform cells of the primitive mesenchyme among which can be found delicate and only partially differentiated fibrils of reticulin. Rarely also a lipoma or fibroma will be encountered, but usually tumors of the meninges resemble in their structure the arachnoidal accumulations or granulations.

The ordinary meningeal tumor is a more or less bulbous mass, separated from the nervous tissue by a capsule of connective tissue, but

adherent to the dura mater. It is composed of cells with abundant dense cytoplasm. The intercellular boundaries are often difficult to demonstrate. The nuclei are oval or elongated with often wrinkled membranes; the chromatin is scanty and collected along the membranes giving the nuclei a vesicular appearance. The neoplastic cells may form a more or less uniform sheet but usually are grouped in masses separated by connective tissue bearing the vascular supply. Within the masses usually no intercellular substances can be found but occasionally reticulin and,

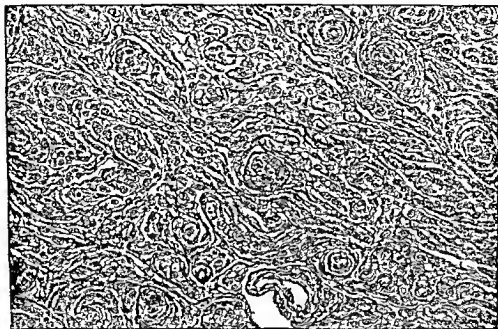


FIG. 61. Drawing of microscopical preparation of a typical meningeal tumor of psammomatous type.

in degenerating areas, collagen is present. The cells of these masses are somewhat elongated and wound around each other to form whorls (Fig. 61). The central cells of the whorls undergo a hyaline transformation and then become calcified. They cause a gritty noise when the tumor is cut, hence their name of psammoma (sand-like) bodies. They are very characteristic of this type of meningeal tumor. The calcification may be followed by formation of actual bone resulting in an osteoma. This bone is of fibrous type not preceded by formation of cartilage. The psammoma bodies are usually formed by deposition of calcium-salts in the center of whorls of cells, as their laminated structure shows, but simi-

lar deposits may occur within the hyalinized walls of small bloodvessels. The endothelium of these vessels proliferates secondarily and undergoes a hyaline change, after which calcium-salts invade the lumen and the resulting calcified nodule is difficult to distinguish from those formed within the cellular whorls. Occasionally the cells of such a tumor are more elongated and form collagen so that the tumor may be spoken of as a fibroblastoma, but the more common type is better called a meningothelioma.

These tumors rarely invade the brain no matter how deeply they may indent it, *but they do not always respect the overlying bone*. In about 25 percent of cases the cranium is invaded (380) by the tumor and this outlet for its growth seems to reduce the pressure inward so that the tumors which have penetrated the bone are as a rule flatter. The meningothelioma penetrates the bone along the bloodvessels and may emerge on the outer surface, elevating the periosteum. The formation of new bone is stimulated and the result is an osteoma above the site of the intracranial lesion. Rarely the cranium is eroded without the formation of new bone. The meningotheliomatous tumors separate smoothly from the cerebral tissue but rarely a bulbous tumor will be found which has a ragged surface and microscopical study shows that the neoplastic cells are advancing into the nervous tissue. These rare tumors in my experience have been composed of a mass of capillaries, so that I have described them as angioblastic (48). They are very bloody and recur rather rapidly after removal at operation. Although the meningotheliomatous type may invade the bones of the cranium and the angioblastic type may invade the brain, these tumors can hardly be spoken of as sarcomatous. They are essentially localized slowly growing tumors which do not metastasize, although rarely more than one may develop in the same patient (281). But other tumors develop from this same leptomeningeal tissue which we may justly call sarcomas (284).

The tumors which we have just described occur on the surface of the brain, although they may indent it so deeply as to be almost hidden within its substance, yet we have seen that the leptomeningeal tissue permeates the brain in every direction. It is true that a tumor of meningothelial type may develop wholly within the brain, but such an occurrence is exceedingly rare. Usually tumors of the perivascular leptomeningeal tissue within the brain develop in such a way as to form cuffs of cells around the vessels. Such a tumor is called a *perithelioma* (25) if it is

relatively benign and the neoplastic cells do not invade the brain but remain confined within the pia-glia membrane. The term perithelioma has been much misused, even for tumors of the brain. In any malignant tumor a perithelial arrangement of the neoplastic cells may result from intervascular degeneration. It should, however, not be difficult to distinguish those tumors in which degeneration has left only cuffs of viable cells from those in which the cuffs of cells are separated by cerebral tissue. Such perithelial tumors vary greatly in structure and malignancy.

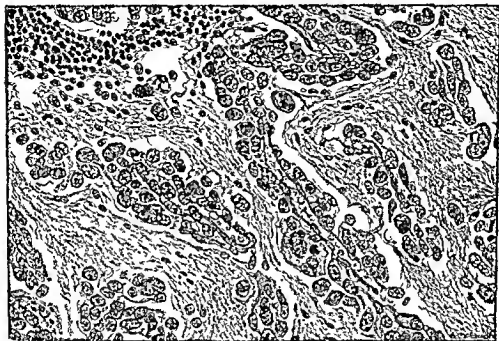


FIG. 62. Drawing of microscopical preparation of a perithelioma. Granular layer of the cerebellum in upper left corner.

At one extremity is found a sort of malformation in which the smaller bloodvessels of the cortex are surrounded by a few swollen rounded cells (Fig. 62). These cells may continue out of the pial funnel and over the surface of the brain; they are then seen to be cells of the intima piae matris. Such an overgrowth is readily differentiated from a pathological infiltration of the perivascular sheath. In the latter case the intima piae matris may be distinguished as a straight line outside the infiltrating cells; in the former there is no pia-glia membrane apart from the hypertrophied cells. In other instances the perivascular leptomeninges forms cuffs which may be many cells in thickness. By study-

ing the boundary next to the nervous tissue one may convince himself that the tumor has not penetrated into the sheaths from the subarachnoid space even though the latter be also involved in the growth. Such tumors may develop at widely different places in the brain and no connection between the foci be found.

The cells of these tumors are peculiar. They are rounded, with considerable cytoplasm and spherical vesicular nuclei. They lie in a loose mass and form very little intercellular substance. As the growth ad-

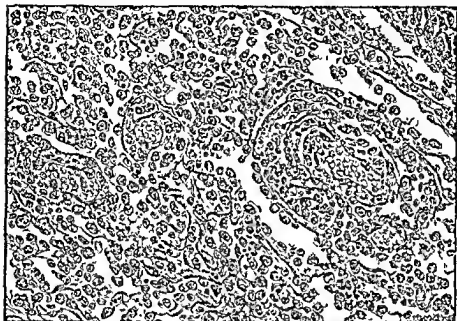


FIG. 63. Drawing of a microscopical preparation of a sarcoma of the brain.
Note the rings of reticulin around the vessels.

vances it can be seen that the nervous tissue between is compressed and degenerates so that areas of tumor become confluent. The blood-supply of the tumor being inadequate because of the abnormal structure of its vessels an intervascular degeneration of the neoplasm may secondarily occur resulting again in a perithelial appearance. When the tumor is found in this last stage it is very readily confused with cellular rapidly growing gliomas in which a similar type of degeneration occurs. The differentiation rests on the structure of the neoplastic cells and on the arrangement of the reticulin (25) which, in the perivascular sarcomas, usually lies in concentric rings around the vessels (Fig. 63). In gliomas

the reticulin radiates from the vessels and the cells of the connective tissue stroma are readily distinguished microscopically from the neoplastic cells. In the rare sarcoma in which the reticulin forms a diffuse network dividing the tumor into alveoli it is quite evident that the reticulin is laid down by the neoplastic cells themselves.

Such neoplastic formations may be confined to the perivascular sheaths within the brain, but exactly similar tumors develop in the leptomeninx over the surface of the brain without involvement of the perivascular tissues or more frequently both may be involved as was the case with the tumor I demonstrated to you. In either case it is usually called a sarcomatosis of the meninges and is often confused with the diffuse infiltration of a malignant glioma called a medulloblastoma. The differentiation is easy in typical cases but may sometimes be very difficult because the medulloblastoma, when it invades the leptomeninx, provokes a considerable overgrowth of connective tissue. True sarcomatosis is predominantly a tumor of adults, whereas we will learn later (page 227) that the medulloblastoma is essentially a tumor of children. In the case of the glioma there is usually also the obvious primary tumor of the brain, while in sarcomatosis any considerable local tumor within the brain is usually lacking. The neoplastic cells are quite different in the two tumors. The cells of the medulloblastoma have very scanty cytoplasm and oval nuclei with abundant chromatin; the cells of the sarcoma are rounded, have abundant cytoplasm and vesiculate, often crescentic, nuclei. The study of the bloodvessels penetrating the brain may aid in differentiation. In the case of the medulloblastoma the neoplastic cells invade the perivascular sheaths, while in the sarcomatosis the perivascular sheaths are transformed into tumor (108).

In discussing the structure of the leptomeninx I postponed mention of the presence of elongated cells filled with granules of melanin. They are found everywhere, even in the perivascular sheaths within the brain, but are most abundant around the medulla oblongata.

It is generally supposed that there are within the body two kinds of melanin-bearing cells, the melanoblasts and the melanophores. The former make their own melanin while the latter obtain it by phagocytosis. The melanoblasts are distinguished by their reaction to diphenylalanine; they are said to be dopa-positive. The reaction depends on the formation of a colored compound by the reagent and certain "premelanotic" substances within the cytoplasm (63). The melanophores lack these formative substances and so are dopa-negative. The melanin-bearing

ing cells of the leptomeninx are dopanegative. Yet it is difficult to imagine the source of their melanin if they do not form it themselves. Perhaps in the early embryonic life they will be found dopapositive as in the case of the dopanegative melanotic cells of the choroidal coat of the eye. If so, their presence in the leptomeninx will constitute presumptive evidence in favor of an origin of the leptomeninx from the neural crest which, at least in lower vertebrates, contains melanotic cells in abundance.

Most of the MELANOTIC TUMORS OF THE BRAIN are metastatic but sufficient cases are now on record to make it fairly certain that a melanoblastoma may arise primarily in the leptomeninx of the brain or spinal cord (199). The microscopical appearance of such tumors is practically identical with that of a sarcomatosis; the cells seem peculiarly liable to an alveolar arrangement. Since these tumors are very rare I cannot show you a patient, but I have here the record of such a case. It is not clinically remarkable; there is nothing typical in the symptoms of these tumors except perhaps the tendency to simulate a chronic meningitis.

The patient (CASE XI) was a man of forty-six years. Having previously been well, he began six months before admission to a hospital to have attacks of dizziness which increased in frequency and intensity until three months later he was obliged to quit work. In the meantime he developed headaches which became excruciating. In the latter part of his illness he was irrational and unable to walk because of weakness and dizziness.

When admitted to a hospital he was very weak and mentally dull. His neck was stiff. The tendon-reflexes were everywhere feeble. There was a nystagmus of amblyopic type, the patient being very myopic. The fundi were not choked and contained no visible tumors. No other signs of organic lesion of the nervous system were found but he was unable to cooperate for a proper examination as he was acutely ill. The pulse-rate was 78 and the temperature 97°. The pressure of the spinal fluid was very high, but was not measured accurately. The composition of the fluid was normal. It was examined for tubercle bacilli and none was found. Shortly after admission he developed a pneumonia and died. A complete examination was made, except for the spinal cord.

Examination of the viscera revealed nothing of importance except bronchopneumonia. There were no pigmented tumors of the viscera. Over the skin no pigmented moles and no areas of pigmentation were

seen. The important findings were intracranial. The surface of the cerebrum was smooth, the convolutions being flattened. Over the parietal region of the left cerebral hemisphere and over the frontal, opercular, and parietal regions of the right cerebral hemisphere were numerous small dark patches. These were numerous also in the interpeduncular region and around the pons and bulb. The nerves of the cerebellopontine angle seemed normal but just where the middle cerebellar peduncle disappears into the left hemisphere there was a black spot about a centimeter in diameter. Section of this hemisphere disclosed a tumor evi-

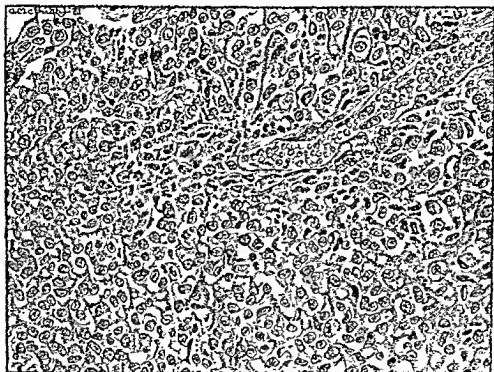


FIG. 64. Drawing of a microscopical preparation of melanoblastoma from CASE IX.

dently extending along the middle peduncle toward the center of the cerebellum to a depth of more than three centimeters. This is surprising because the hemisphere externally did not seem enlarged or distorted. The cut surface of the tumor was ragged and almost black; it was fairly sharply circumscribed. The ventricles of the brain were dilated moderately; there were many cysts of the choroid plexuses of the lateral ventricles. Although it is unusual for such a large extension into the brain to occur in these cases there seemed no good reason from gross

examination to suppose that the tumor was not primarily intracranial, arising from the melanoblasts of the leptomeninx.

Microscopically the main mass of the tumor is composed of polygonal cells arranged into alveoli by others which are more elongated. The elongated cells form reticulin, the alveolar cells do not. There is a very little collagen around some large bloodvessels. The structure is typical of an alveolar sarcoma. In some areas all of the cells are fusiform and here the tumor resembles a spindle-celled sarcoma (Fig. 64). Mitoses are numerous. Within the cells of both the alveoli and stroma

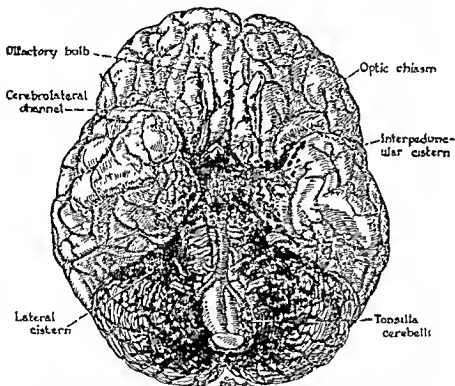


FIG. 65. Brain with melanoblastoma of basal leptomeninx (after Schopper)

are abundant granules of melanin. The pigmented spots over the brain prove to be isolated nests of melanoblasts, either in the leptomeninx or within the cortex in the leptomeningeal sheaths of the bloodvessels. There seems to be no connection between these foci of pigmentation. It looks as if there had existed numerous areas of overproduction of pigmented cells in one of which a malignant transformation occurred.

The tumor is unquestionably a melanoblastoma arising in the leptomeninx.

It is difficult to distinguish the melanoblastoma from the other sarcomas of the leptomeninx except by the presence of melanin in the cells. They are most probably all essentially identical tumors. Melanosarcomas occur usually over the base of the brain (188) and spread widely in the leptomeninx (Fig. 65). They are easy to recognize by their gross appearance. There is no distinctive symptomatology of intracranial sarcomas which would enable one to make a pathological diagnosis during life. While theoretically possible to make by biopsy, or perhaps by the finding of neoplastic cells in the spinal fluid, it has never been made antemortem to my knowledge. When the tumor is fairly localized it may cause symptoms of a lesion of that part of the brain, usually, however, the tumor is so diffuse that the only presumptive diagnosis possible is intracranial tumor, unlocalizable. *Many cases are suspected of being tuberculous meningitis.*

There is no effective THERAPY at present for these sarcomatous tumors. They are important mainly from the standpoint of theoretical pathology. Perhaps roentgen radiation might be helpful. The bulbous encapsulated meniotheliomatous tumors, on the contrary, are often readily and completely removed. We will study them in more detail from the clinical point of view.

CHAPTER 8

MENINGIOMAS.

SYNDROMES OF THE CENTRAL REGION, THE OLFACTORY GROOVE, THE SPHENOIDAL WING, AND THE SELLAR TUBERCLE

Of all the tumors of the meninges the most frequent and most important to recognize clinically is the bulbous encapsulated type now generally spoken of as a *meningioma*. Since this tumor compresses the nervous tissue without invading it, removal is usually followed by practically complete restoration of nervous function. This was first successfully accomplished, to my knowledge, by the Italian surgeon Durante in 1884, and the most striking successes of neurological surgery still are those obtained by operations for these tumors. Their removal, how-

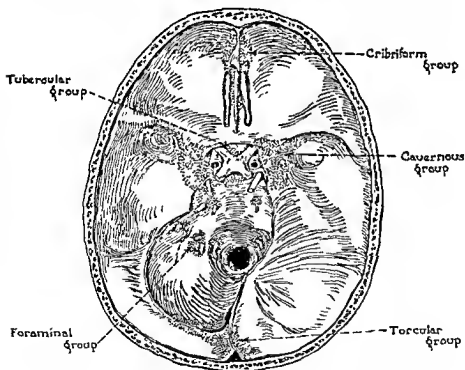


FIG. 66. Location of the arachnoid granulations over the base of the skull (after Aoyagi and Kyuno).

ever, is peculiarly hazardous and demands all the knowledge and resources of the surgeon for its successful accomplishment.

We have already noted the resemblance of the microscopical structure of meningiomas to that of the arachnoidal granulations. The prob-

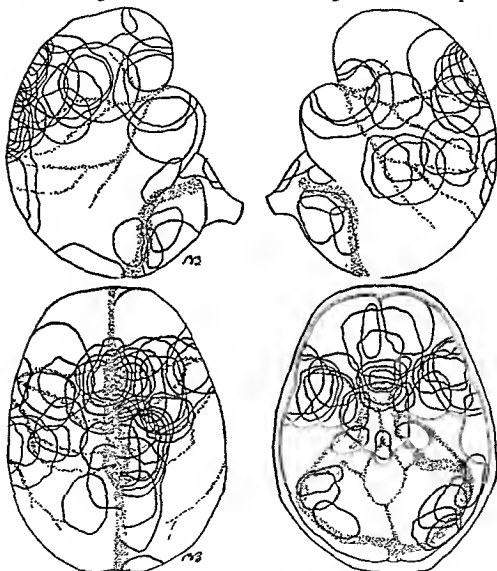


FIG. 67. Distribution of a series of meningiomas over the surface of the meninges (after Cushing).

ability that meningeal tumors arise from these bodies is increased by the demonstration that the distribution of these neoplasms within the intracranial cavity is approximately that of the arachnoidal granulations which

project into the venous sinuses and lacunae of the dura mater. They are particularly numerous in the central region near the superior longitudinal sinus in the inner walls of the great parasagittal lacunae. Here they may be found as early as the third year of postnatal life and increase in number with age. In old age they spread laterally along the middle meningeal veins. They are fairly numerous also along the basilar sinuses

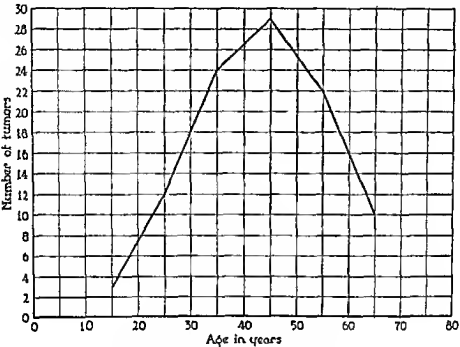


FIG. 68 Age-distribution of meningiomas.

(Fig. 66) especially over the cribriform plate, over the tuberculum sellae, along the sphenoidal and cavernous sinuses and the transverse sinuses on the cerebellar surface near the torcular (104). Some are found in the foramina of exit of the cranial nerves of the posterior fossa, over the clivus, and along the sphenoparietal and straight sinuses. They tend to congregate in the regions where the cerebral veins open into the sinuses. The DISTRIBUTION OF MENINGIOMAS is very similar (125). Although occasionally such tumors may occur anywhere over the convexity or poles of the cerebrum, or along the falx cerebri, the vast majority are concentrated in the parasagittal central region (Fig. 67). From here they scatter down the course of the middle meningeal veins to a new concentration in the cribriform, tubercular and sphenoidal regions. A

few more are scattered along the transverse sinuses and near the foramina of the cranial nerves.

Although the meningiomas in these various localities have features in common the clinical syndromes which they cause are quite different and sufficiently distinctive to merit separate description. They all agree in this, however, that they are tumors of adult life as shown by the chart of their age-distribution given in Fig. 68.

The *PARASAGITTAL* region in the neighborhood of the great venous lacunae of the dura mater is a favorite site of origin for meningiomas. Perhaps one in every four will be found in this situation. It is, therefore, important that the peculiar manifestations of this group be clearly understood. The usual meningeal tumor over the convexity of the hemispheres is a rounded mass varying in diameter according to the stage of its development. Its surface is smooth or only grossly nodular and sharply circumscribed, consisting of a dense sheet of collagenic tissue. It is attached almost invariably to the dura mater over a greater or lesser extent, sometimes of course to the wall of a dural sinus or lacuna. Rarely the tumor near its attachment to the dura mater may spread in a thin sheet for a short distance along the under surface. The tumor indents the surface of the cerebral hemisphere deeply, pushing the cerebral tissue before it, displacing the convolutions and altering their relationships (Fig. 69). Because the cerebrum is compressed gradually it has time to accommodate itself and herniates into every possible corner of the intracranial cavity, displacing the cerebrospinal fluid and obliterating the subarachnoid space. Even the great dural septa may give way to a certain extent but usually their edges cut deep grooves into the cerebral tissue and in this way cause misleading symptoms, the most frequent example of which is the production of a homolateral hemiparesis by pressure of the incisura tentorii upon the contralateral cerebral peduncle (298).

Into the surface of the tumor large veins and arteries enter from the adjacent pia mater. The veins often open widely into the dural sinuses and the tumor is so intimately connected with them that its removal may be hazardous or impossible. The tumor may penetrate into or through the cranial vault so that its complete removal may necessitate removal of the overlying bone and subcutaneous tissues. Rarely the surface of such a tumor is ragged and separates with difficulty from the cerebral tissue; in these cases the tumor is found to be of angioblastic or sarcomatous type.

I have already remarked that these large bulbous meningiomas are usually meningotheiomatous or psammomatous in type. Such a tumor has been removed from this man (CASE XII) of thirty-seven who was always well until four years ago when he had an attack of twitching of the right hand, arm, and face. He did not lose consciousness, the twitching lasted only a few moments and he forgot about it until it returned a month later. Similar attacks recurred with increasing frequency. Four months after the onset he began to limp a little with

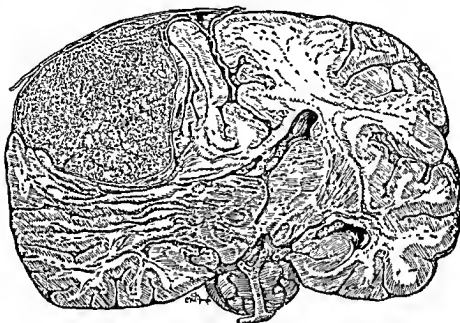


FIG. 69. Cross section of brain with meningioma in place.

the right leg although there had never been any twitching of the leg; two months later for the first time the right leg also was involved in a severe attack which began with an indescribable sensation in his right arm. A physician was called who pronounced it a "nervous breakdown." After this attack the right arm continued to be very weak and felt numb; the right leg was also a little weak. Strength returned slowly so that within six months he could write with his right hand. But soon he lost consciousness for the first time in an attack, and continued in this way with frequent convulsions for nearly a year. Up to this time he had been working as manager of a chain-store. He did his work well and there were no complaints. But now he lost ambition.

Two years ago he went to a veterans' hospital and was given luminal for the first time, with prompt suppression of the attacks for an entire year. But about six months ago he noticed for the first time difficulty in speaking. He understood what was said to him but could not find the proper answer. A month later he had a mild convulsion and continued to have them about once a month. His right arm and leg grew steadily weaker. He had difficulty in calculating, whereas formerly he was noted for his ability in mental arithmetic. Two years ago he noticed that his vision was hazy. Glasses were prescribed. Six months later the glasses were changed because of the same trouble. Lately the haziness was much worse. He never complained of headache and never vomited.

Finally, last month, a new consultant to the hospital seems to have been the first physician to suggest that he might have an intracranial neoplasm and sent him to this clinic. When admitted he seemed quite well. He was alert and coöperative. He stated that if the doctors did not quit asking him about his headache he would finally have one. There was a right spastic hemiplegia, the face and arm being much more involved than the leg. There was a complete astereognosis of the right hand. Tactile discrimination, tactile localization, sense of position, of passive motion, and vibratory sense were grossly disturbed over the entire right side of the body, especially the hand. There was an agnosia of the fingers of the right hand. He had great difficulty in expressing his thoughts but understood well what was said to him and read well. He could not calculate. There was a right homonymous hemianopia with sparing of the maculae. The visual acuity of the right eye was 0.4 and of the left 0.2. The right optic disc was slightly blurred along the nasal margin but not swollen and apparently otherwise normal. The left disc was swollen about 2.5 diopters and its margins were completely obliterated; there were numerous dilated capillaries over this disc but no hemorrhages. Roentgenogram of the head revealed no pathological alteration of the cranium except some decalcification of the sella turcica.

The clinical impression was of an extensive benign tumor of the left cerebral hemisphere, probably a gliomatous cyst. A left osteoplastic exploration was made and after a struggle of five hours there was removed a meningeal tumor weighing 203 grams (Fig. 70). Only a small area of this tumor was visible on the surface of the brain just lateral to the sagittal sinus, possibly 2.5 cm. in diameter. The tumor lay almost entirely subcortically and was adherent to the falx cerebri.

It was necessary to transect the cortex for a distance of five centimeters anterior to and parallel with the precentral sulcus in order to deliver the growth. His right arm was totally paralyzed for several days and his speech reduced to a few words. His stereotyped reply to any question was "fine." Gradually a few other words returned. It is now a month after operation. He has great difficulty in speaking and writing but understands and reads well. But I do not want to insist now on his difficulty of speech. We will examine that at a later date. Today we will

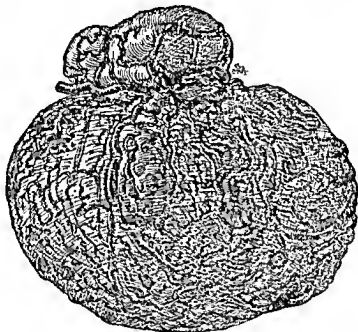


FIG. 70. Tumor removed from CASE XII. Natural size.

analyze his hemiplegia. First let us state that the sensory loss has been largely regained. He recognizes his fingers but has difficulty in recognizing objects in his right hand. Part of this trouble is caused by the spasticity and paralysis of his fingers which prevent him from manipulating objects placed in the hand. Tactile discrimination is fairly good and vibratory sense is present. Sense of position also has returned. The hemianopia has disappeared.

The patient walks with the right lower limb held stiffly in extension. Because of the extension of the ankle the limb is too long and, since the patient cannot in walking flex either the knee or ankle, the only

motion is at the hip so that he is obliged to swing the limb outward in bringing it forward, usually dragging the great toe on the floor. This is the usual gait of a spastic hemiplegic patient. We will now ask him to lie on his back and examine his reflexes. You will note that the right triceps, biceps, and radial reflexes are very brisk and there is a very marked and persistent clonus of the wrist. The knee and ankle jerks on the parietic side are also much exaggerated; there is an extensor plantar reflex and a clonus of the ankle.

The position of the limbs in this patient is the classical position in a HEMIPLEGIA OF CEREBRAL ORIGIN. The shoulder is slightly lifted; the arm is adducted and rotated inward; the forearm is moderately flexed and pronated; the wrist is flexed; the thumb also and the fingers over it. In the lower limb the hip is adducted and slightly flexed, the knee extended and the ankle extended plantarward and slightly introverted; the great toe is strongly dorsoflexed. When we examine his limbs, and try to move them passively, we find that they are maintained in this position by powerful tonic contraction of the muscles, particularly of the trapezius, the pectoral muscles, the biceps, the pronators and the flexor muscles of the forearm and fingers. In the lower limb the spasticity affects especially the quadriceps femoris, the soleus in the leg, and the internal rotators of the foot. The muscles of the face, trunk, and pelvis are not contracted.

It is difficult to form a true estimate in our patient of the voluntary muscular power because the action of many of the muscles is hindered by the powerful tonic contraction of their antagonists. But in cases of recent hemiplegia from cerebral softening there is often a period before the onset of spasticity when the true loss of voluntary power is more easily determined. The paralysis in general is more marked in the periphery of the limbs and more profound in the upper than in the lower limb. In the upper extremity elevation of the shoulder is feeble, adduction and external rotation are weak, internal rotation is little affected but abduction is impossible. Extension of the elbow is weaker than flexion and supination is impossible. In mild cases flexion of wrist and fingers may persist while extension is badly affected. In the lower extremity flexion and abduction of the hip are weakened. The posterior muscles of the thigh are more affected than the anterior. Dorsiflexion of the ankle is impossible but extension is retained. The external rotators of the foot are more affected than the internal rotators. In the lower limb the weakness seems least pronounced in those mus-

cles which later became most spastic; in the upper limb exceptions to this rule occur, notably the trapezius.

In a hemiplegia the cranial nerves largely escape. Movements of the eyes are normal; the masticatory muscles are affected slightly if at all, and then only transitotily. The face is usually weakened only in its lower portion. The pharynx is normal. The tongue retains its motility and only deviates somewhat to the paralyzed side when it is pulled far forward by the genioglossus muscle. The trapezius muscle is paralyzed but the sternocleidomastoid muscle escapes. The abdominal and dorsal muscles are also largely intact.

If we now examine our patient we find that elevation of the right shoulder is weak. He cannot abduct the arm but can drag it feebly toward the chest. The elbow is flexed weakly but cannot be extended. He is unable either to pronate or supinate the forearm, and cannot either flex or extend the fingers. The greatest degree of paralysis is in the distal part of the extremity as is commonly the case. The distribution of the paralysis seems, therefore, to be quite different from that I have just described as typical of the flaccid stage. The difference is more apparent than real, for paralysis of the forearm and hand in this case is total and the extension of the elbow and abduction of the arm are checked by the powerful spastic contraction of the biceps and pectoral muscles. In the right leg, where the spasticity is less, it is possible to demonstrate that the greater weakness is of the hamstring muscles, the dorsoflexors of the foot, and the extrovertors of the ankle.

But although the patient is unable to contract voluntarily many of the muscles, and the action of others is greatly hindered by the spasticity of their antagonists, still reflex contractions of these muscles occur in what are known as *associated movements* (332). These can be readily demonstrated. When he grips forcibly my hand with his left hand you note that the right arm rises from the bed, is abducted, the elbow flexed and the wrist slightly flexed and supinated. The movement was slow, began after a distinct latent period, and the position of the limb was maintained until the grip of the left hand was relaxed. The right leg did not move during this time, but the right great toe was extended. If the lower extremity were more spastic it would also be extended at hip, knee, and ankle and the foot slightly introverted. In this reaction the fingers moved little but the patient himself has remarked that, although he is unable voluntarily to extend the fingers, when he yawns they extend completely. At the same time the arm is abducted and the

forearm flexed. When a patient with a slighter paresis voluntarily lifts his paretic arm with a great effort above his head the fingers may also at times extend.

We sought for these reactions with the patient in bed in the recumbent position, the head being in the midline, the patient looking at the ceiling. They are practically constant for the same patient when sought for in the same position, but they may be varied in definite ways (493). For example if I turn this patient's head now strongly to the right so that he faces the paretic side nothing happens to the limbs, but if he grips forcibly with his left hand the right arm is abducted as before although the elbow is extended. With the head facing the sound side a prompt and complete flexion of the right elbow is obtained. In more favorable cases the mere forcible rotation of the head over to the paretic side may cause the paralyzed arm to be advanced and adducted, the forearm pronated, the wrist extended and the fingers tightly clenched. Similarly, rotating the face to the sound side may cause an exaggerated flexion of the paralyzed arm. The effect of these manipulations of the head and neck are not very evident on the paretic leg.

Another reaction shows clearly the importance of the other parts of the body on the position and reactions of the paralyzed arm (72). If this patient is made to bend forward, while I hold him by the hips, until the extensor muscles of the hips and spine no longer support the weight of the trunk, the flexor position of the upper limb changes. It is moved toward a position perpendicular with the body, adducted and internally rotated, the forearm changing from flexion to rigid extension. It is also increasingly pronated. The wrist and fingers remain flexed. This reaction is rare in my experience but in this patient it is very characteristic.

Similar associated movements are more difficult to elicit in the paretic lower extremity, partly because it is ordinarily less spastic, the spasticity seeming to be a necessary accompaniment of these associated movements. If a patient with a spastic leg is asked to flex his sound foot strongly against resistance the paralyzed one extends plantarward and the toes flex. Again if, with the patient in the sitting position, he is told to adduct his sound knee against resistance, the paretic knee adducts. Similarly it can be made to abduct. In our patient these reactions cannot be obtained. Other characteristic reactions, however, are present in the lower extremities. We note that the patient cannot lift simultaneously the two legs, although he can lift either alone. Although vol-

untary dorsoflexion of the right foot is impossible, when the hip and knee are flexed the foot also is dorsoflexed. Moreover, he is unable to flex the right hip without simultaneously flexing knee and ankle. The face does not participate in these associated reactions.

Hemiparesis plays a large rôle in the symptomatology of intracranial tumors and it is necessary that the student be familiar with this symptom. It is evident that not all the muscles in one half of the body are paralyzed in a so-called hemiplegia and we have seen also that many of those which cannot be contracted voluntarily may be made to contract powerfully by reflex reactions. The muscles are capable of contracting but the volitional mechanism for throwing them into action has been deranged. It has been amply demonstrated that an injury which causes this symptom always interrupts the great corticospinal projection-pathway in part or entirely. It is unquestionably the medium of what we call voluntary muscular contraction. The powerful tonic involuntary contractions of certain muscles and the associated reactions just described make it certain that there are other, so-called extrapyramidal, motor pathways to the muscles of the limbs.

The details of the CORTICAL PROJECTION-SYSTEM are not sufficiently known to enable us to explain the distribution of paralysis in hemiplegia on the basis of anatomical connections. The fibers of this system arise from the middle part of the cerebral hemisphere and none of them comes from the occipital lobe or angular gyrus nor from the anterior three-fourths of the frontal lobe. From the upper five-sixths of the anterior central gyrus the fibers pass through the posterior segment of the internal capsule, those of the upper extremity lying most posteriorly; most of them pass downward through the middle segments of the cerebral peduncle and through the bulbar pyramid to the inferior part of the bulb. Some of the fibers here curl around the inferior olive and continue downward on the same side in the anterolateral part of the lateral column. These are called the homolateral pyramidal fibers. Others continue down into the ventral column of the same side. These form the direct or uncrossed pyramidal tract. But a considerably larger portion of the fibers cross in the lower part of the medulla oblongata and continue down into the dorsal part of the lateral column of the opposite side, the indirect or crossed pyramidal tract. While the lateral crossed fibers go to both heterolateral extremities, the direct pyramidal tract ends in the dorsal region.

The fibers from the posterior frontal region, especially from the

posterior extremity of the superior and middle frontal convolutions, pass downward through the knee of the internal capsule and the internal fifth of the cerebral peduncle to end largely in the pontine nuclei of the same side. The fibers from the posterior part of the temporal lobe, especially from the cortex of the middle and inferior temporal convolutions, pass downward in the sublenticular part of the internal capsule to go via the external fifth of the cerebral peduncle largely to the pontine nuclei of the same side. This is the *temporopontine tract* (of Tuerck) (cf. Fig. 29). In the middle part of the cerebral peduncle there must also be a certain number of fibers coming from the parietal cortex and destined also for the pontine nuclei. Their exact course is not well known. In addition to all these there are a great number of aberrant fibers arising from the operculum around the lateral fissure and destined for the intercalated system of the peduncle and bulb. Through them the motor nuclei of the cranial nerves are innervated. This whole system in the midbrain forms what is known as the *pedunculus lemnisci*, a continuous line of fiber-fascicles which proceed from all parts of the cerebral peduncle to the medial lemniscus along the caudal pole of the substantia nigra (476).

Probably in very few instances do any of these long projection-fibers come into relationship either with the motor nuclei of the bulb or of the spinal cord directly. Perhaps a few rare fibers reach directly the 7th and 12th nuclei. The others must end upon intercalated neurons. The intercalated systems are certainly much more extensive in the bulb than they are in the spinal cord, but probably also in the cord the corticospinal fibers end on intercalated neurones. This makes it impossible to demonstrate that the nuclei of certain muscles are connected in the bulb and spinal cord with the projection-system while others are not, for the degeneration of the interrupted fibers always stops short of the motor cells. We must suppose, however, that some nuclei are innervated from both cerebral hemispheres, otherwise it would be impossible to explain why the upper facial, masseter, lingual, palatal, and abdominal muscles escape the voluntary paralysis. The paralysis of the lower extremity is less profound probably because it functions much more automatically than the upper extremity and receives fewer voluntary fibers; we have noted that the direct pyramidal tract does not reach the lumbar enlargement of the spinal cord.

Our patient then has a fairly typical spastic hemiplegia due to interruption of the corticospinal pathway. But the order of development

of the symptoms was not the usual one occurring with a parasagittal meningioma. In this case the tumor was subcortical and involved the tract where it converged into the internal capsule. But meningiomas usually develop from the arachnoidal granulations in or near the parasagittal lacunae as we have seen. The tumor then presses first on the cortical area for the foot so that the epileptic attacks, later the paralysis, begin in the foot, subsequently involve the leg, then the arm, and finally the face. *Such a course of events is very characteristic of a meningioma and is rarely caused by any other type of tumor.*

The epileptic attacks beginning in the contralateral foot and gradually involving the leg, then the arm, and the face, at first without loss of consciousness, later with loss of consciousness, and the hemiparesis beginning with weakness in the foot, transitory at first following the attack but later permanent, are readily explained from what we have already learned of the structure and function of the central region of the brain.

If the tumor arises primarily behind the anterior central gyrus the epileptic attacks may not be of the typical kind described. The attack may be initiated by an abnormal sensation in the opposite side of the body, primarily in the foot, and muscular movements develop later, if at all. This preliminary abnormal sensation, or aura as it is called, consists usually of a tingling, burning or numb feeling in a certain localized region of the body (in this case the foot) which gradually spreads to adjacent parts of the same side, followed by muscular movements and loss of consciousness in severe attacks. When the tumor lies still farther back along the sagittal sinus, or forward in the precentral region, the attacks differ again in character and are apt to be generalized from the beginning or initiated by a turning of the eyes and head to the opposite side with torsion movements of the extremities.

Sooner or later, depending upon the exact relationship of the tumor to the central sulcus, loss of sensation is also noticed on the opposite side of the body. This loss predominates first in the lower extremity and involves the proprioceptive to a greater extent than cutaneous sensibility. The sense of position and vibratory sensibility are lost early in the lower extremity, particularly in the foot and leg, also tactile localization. Rarely there may be considerable atrophy of the musculature of the opposite half of the body with a tumor lying far back in the parietal region (439). When the tumor lies anterior to the anterior central gyrus there is often added another symptom which is known as

forced grasping and groping. (1). If an object is placed in the patient's hand it is firmly grasped. An attempt to remove the object only causes the patient to grasp it more firmly and he has considerable difficulty in voluntarily relaxing his grasp. All of these symptoms may appear, and usually do appear, before there is any evidence of increased intracranial tension. By the time headaches and vomiting and choking of the optic discs have appeared the tumor has reached a tremendous size.

Objective external evidence of the presence of a tumor may be visible. It is often possible to see that the extracranial bloodvessels are greatly dilated and tortuous. Moreover *a tumefaction of the skull may be seen.* (Fig. 73). This area may or may not be tender to pressure, is smooth and rounded, ordinarily quite firm and hard throughout, although in rare instances the center of the elevation may be softened. The patient may be quite oblivious of this protuberance, or his attention may early have been called to it by the fact that it was sensitive when he washed his head or combed his hair. Sometimes the patient's attention is attracted to it by a blow on the head which, if it lands in this particular region, produces an exaggerated effect and a more or less lasting soreness.

These tumors in the early stages must be diagnosed from all other conditions which cause focal epilepsy. Since they occur usually in middle age the diagnosis is to be made from syphilis of the brain, vascular lesions, or the common type of glioma which we will describe later under the name of glioblastoma multiforme. Focal epileptic attacks may occur in cases of gumma but these lesions are now, since lues is so thoroughly treated, quite rare. A gumma may usually be differentiated, of course, by other concomitant signs of lues and by the serological reactions, in case there is no history of luetic infection. Arteriosclerotic lesions are usually accompanied by the acute symptoms of a vascular insult, namely sudden headache and transitory loss of consciousness. Symptoms come on therefore suddenly and tend to improve, whereas in case of a meningeal tumor the symptoms are slowly progressive. Symptoms of cardiovascular disturbance may also aid in making the differentiation. It should not be forgotten that the patient may have lues or arteriosclerosis of the cerebral vessels, or both, and also have a meningeal tumor.

The positive DIAGNOSIS of *meningeal tumors* is made on the basis of the characteristic slow progression of the symptoms plus the local alterations in the cranium. These alterations may be palpable or they

may be demonstrated only by means of the x-rays (452). In the latter case one sees both erosion and formation of bone. The erosion is a localized thinning which is irregular in outline and spongy. The bone on the other hand may be thickened and either denser or lighter than the surrounding cranium. On the surface of the bones of the cranial vault may appear perpendicular spicules (Fig. 71). Rarely the bone may be eburnated like an osteoma. The typical change, however, is a mixture of rarefaction and proliferation of bone, doubtless due to the fact that the

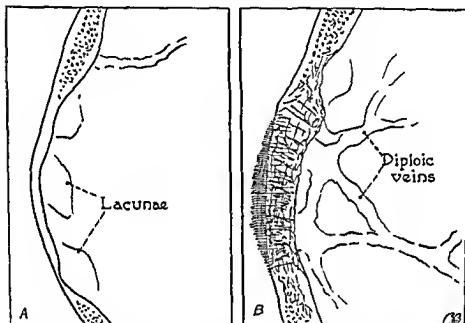


FIG. 71. Schemes from two roentgenograms of the parasagittal region. A—erosion by parasagittal lacunae; B—erosion, thickening, and formation of spicules by a meningioma. Compare Plate v.

tumor penetrates into the Haversian canals, stimulating the formation of bone which it later destroys. As it penetrates through the outer table of the skull the periosteum is elevated and forms bone between the advancing columns of neoplastic cells. There is often visible also in the neighborhood of the tumor a great dilatation of the vascular markings of the skull. The middle meningeal arteries and veins, more particularly the veins, on this side are larger; diploic channels are enlarged. The depressions formed by the venous lacunae are exaggerated and the emis-

sary vessels are also enlarged. This enlargement of the diploë means very little unless it occurs in the area toward which symptoms point, is not present on the opposite side, and there is no general dilatation of the diploic channels (184). *One should be careful also not to mistake the depressions in the inner table of the cranial vault caused by the venous lacunae for the erosion of a tumor.*

MENINGIOMAS ARISING FROM THE TUBERCULUM SELLAE are rare but cause a characteristic syndrome so that they deserve special notice. This patient (CASE XIII) is a woman of forty-two years. She has had uniformly good health all of her life, except for a tendency to headaches. Six years ago she first noticed some trouble with vision, but it was not until later that she was sufficiently troubled to consult an oculist, who prescribed glasses. From this time the failure was more rapid, and the vision on the right had become greatly impaired. Under the impression that she was suffering from the effects of some toxic process, a lumbar puncture was made, and finally an operation on the gallbladder was advised. This was refused, and she was put on a diet. Later she took a "cure" at Hot Springs. Subjectively a bitemporal loss of vision was appreciated.

When examined in another clinic five years ago she was found to be a well-nourished woman with wholly negative physical and neurological findings apart from the eyes. The optic discs had a marked pallor of atrophy. There was a typical and fairly symmetrical bitemporal hemianopia though vision was most affected in the left eye, the acuity being only 10/100 compared to 10/70 on the right where there was greater constriction of the field. The olfactory sense was unimpaired. The sella turcica was essentially normal in size, shape, and position. There were no secondary hypophysial symptoms. The basal metabolic rate was —3 percent. A diagnosis of probable suprasellar meningioma was made and under local anesthesia a frontal osteoplastic operation disclosed a nodular tumor about 2 cm. in diameter in front of the optic chiasm. The tumor was readily exposed, and its anterior portion was excavated until its attachment to the tuberculum sellae was freed. Finally, the loosened posterior shell of the growth was lifted out in its entirety. The fragments of tumor weighed 13 grams. Sections showed the tumor to be a typical meningioma.

Within three days the patient was conscious of distinct improvement in her sight with perception of objects in both of the previously blind temporal fields. Improvement was continuous so that a month later

the visual fields were considerably expanded. It is now four years and eight months since her operation. She has grown somewhat stouter but is otherwise quite well. Visual acuity in the right eye is 0.8 and in the left eye 1.0—2. There are still some relative scotomas in the right lower quadrant of the right eye and an irregular defect in the right lower quadrant of the left visual field, but her vision has continued steadily to improve and there is no reason to suppose that there is any recurrence of the growth.

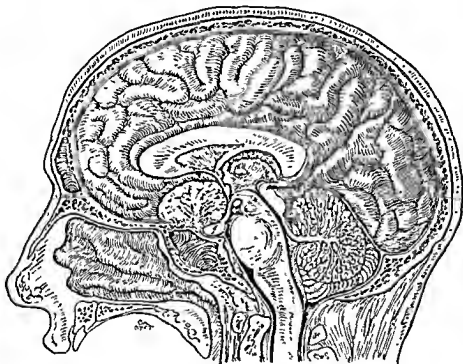


FIG. 72. Median section of the head with a meningioma of the tuberculum sellae in place.

Suprasellar meningiomas have been examined postmortem in all stages of development. The tumor unquestionably arises from the region of the tuberculum sellae, and expands upward, lifting the optic chiasm upward and backward (Fig. 72). As it increases in size the optic nerves are separated and stretched. With still further increase the olfactory bulbs are compressed and the tumor pushes backward and over the sella turcica and upward into the hypothalamus and base of the frontal lobes. The tumor has a rounded dome. Its surface is knobby like that

of a golfball. It is usually relatively avascular but may involve in its growth the cavernous sinus, the anterior cerebral arteries, the ophthalmic, or even the internal carotid arteries, so that when it reaches a certain size its complete removal may be hazardous or even impossible.

This patient came to operation in a favorable stage of the development of her symptoms. When the tumor is small the only symptom is the bitemporal hemianopia which is rarely symmetrical as in the case of a hypophysial adenoma. As the pressure on the optic nerves increases the optic atrophy may increase to complete blindness; usually, however, one nerve resists for many years. As the tumor increases in size also an anosmia is likely to be added to the symptoms and some slight alteration of the sella turcica occurs—a deficiency of the anterior clinoid processes or a flattening of the sella as a whole. When the tumor has reached a considerable size there may be marked mental deterioration, sufficient to cause internment in an asylum. Rarely there may be a slight hemiparesis, uncinatc seizures, polyuria, amenorrhœa, frontal or bitemporal pain, or oculomotor palsy from pressure on adjacent nervous structures. Even in the terminal stages of the tumor the symptoms of general increased intracranial pressure are absent.

The *diagnosis* of a meningioma of the tuberculum sellae is made when a middle-aged patient develops a bitemporal defect of the visual fields and primary optic atrophy, if the sella turcica is normal and there are no signs of involvement of the hypophysis or hypothalamus (143). This diagnosis may be erroneous; the syndrome may be produced by either an adenoma or craniopharyngioma, but rarely. Ordinarily an adenoma will cause, as we have learned, a ballooning of the sella along with the bitemporal defect in the visual fields and symptoms of hypophysial deficiency. In only very rare instances will a hypophysial adenoma rupture the diaphragm early and cause purely a bitemporal visual defect. The craniopharyngioma will cause difficulty in diagnosis only in adults. Often with these tumors there is little change in the sella turcica, but the suprasellar calcification, the choking of the optic discs, the adiposity, polyuria, or other hypothalamic or hypophysial symptoms usually suffice to establish the correct diagnosis. The glioma of the optic chiasm should rarely confuse. It is a tumor of children or young adults. There is almost never a bitemporal defect of the visual fields. Dilatation of the optic foramina will often establish the correct diagnosis. The appearance of the optic discs also is rarely that of a pure primary optic atrophy. In rare instances a local chronic arachnoiditis has possibly

caused a similar clinical condition (112).

The meningiomas of the tuberculum sellae in all probability arise from arachnoidal granulations in the anterior communicating branch of the cavernous sinus. Similar tumors may arise from any part of this sinus and, when posteriorly situated, may cause early involvement of the trigeminal nerve with a resulting neuralgia in the face (204) but most commonly these tumors seem to arise along the lesser wing of the sphenoidal bone. Here they give rise to a fairly characteristic SYNDROME OF THE SPHENOIDAL RIDGE which the following patient has fully devel-



FIG. 73. Patients with meningiomas. At left CASE XIV with unilateral exophthalmos; at the right, patient with a parasagittal exostosis

oped. It was such a meningioma doubtless which Durante removed in 1884.

The patient (CASE XIV) is a housewife forty years of age, previously well, who noticed twenty months before her admission to this clinic that her eyes tired when she read or sewed for any length of time. Shortly afterward she found that the difficulty was with the right eye and that if she kept the left one closed her vision was blurred. About the same time a friend remarked that the right eye was more prominent than the other (Fig. 73). The eye was never painful nor was there ever any headache. The right eye gradually became more prominent. She is a very healthy and robust woman. When admitted to the hospital the only abnormality found concerned the right eye. There was a very

pronounced right exophthalmos; right 20, left 13. The vision in this eye was reduced to 0.5—2. The external ocular movements were normal and so were the reactions of the pupil. The fundus oculi was normal. The visual field was generally contracted. Nothing could be felt in the orbit. The right temporal region seemed fuller than the left. Roentgenogram revealed on the right side thickening and increased density of the sphenoidal wings, the lateral wall and part of the roof of the orbit and both borders of the superior orbital fissure almost to the optic foramen (Fig. 74).

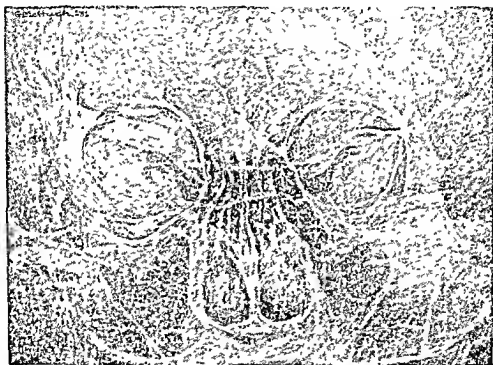


FIG. 74. Drawing from roentgenogram showing thickening of right orbito-sphenoidal region of the skull (CASE XIV). Compare Plate IV.

A diagnosis was made of meningeal tumor invading the bone. The lesion was approached by an incision curving upward from the outer angle of the right eye then backward and downward to the zygoma just in front of the tragus. The superficial tissues were stripped downward. There was found a small elevation of the bone low down in the temporal fossa; it was later proved that this exostosis contained tumor. All of the thickened bone was removed with a rongeur. The dura mater

was then opened and a mass of tumor about 3 cm. in diameter and 2 cm. in thickness was found, just back of the superior orbital fissure, indenting the tip of the temporal lobe. It was removed with the attached dura mater. A week later a rounded mass about 2 cm. in diameter was removed from the orbit through the same incision. Except for massive edema of the orbital tissues and a paralysis of the right sixth nerve there were no complications. It is now a month after operation. The paralysis

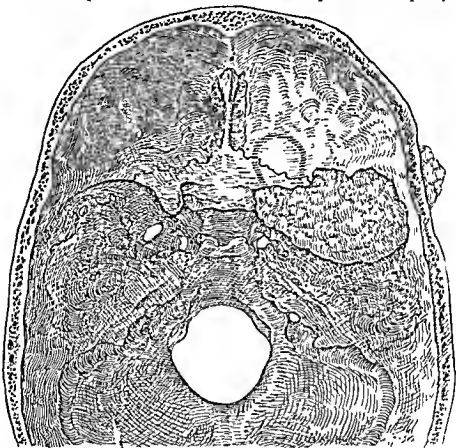


FIG. 75. Base of the skull with a meningioma of the sphenoidal ridge which has penetrated to the temporal region of the skull and extended into the orbit.

of the right sixth nerve persists and there is still some edema of the right eyelids. The exophthalmos persists and the visual acuity and visual fields are practically the same. She feels perfectly well and the wound is healed.

As found at operation or necropsy (Fig. 75) these meningiomas of the sphenoidal ridge have a tendency to be flattened, cover a considerable area of the internal surface of the skull and invade the bone actively, usually with a resultant densification visible in the roentgenogram (121). The tumor may erode the bone or penetrate it and appear in the orbital cavity or temporal fossa. When the tumor lies near the sella turcica the latter may be somewhat eroded. The olfactory nerve may be pressed upon or the homolateral optic nerve primarily involved. With increasing size the eye-muscle nerves are invaded and even the trigeminal nerve.

Most prominent among the symptoms is a unilateral exophthalmos which slowly develops over a period of years. The eye does not pulsate and is not painful to pressure. It usually moves freely in every direction but there may be palsies of the eye-muscle nerves. There is usually some edema of the eyelids and conjunctiva. Ordinarily there is no defect in the visual fields and the fundus oculi is unchanged. Late in the course of the disease some swelling of the optic discs may occur. The other common symptom is a slight bulging of the temporal region on the side of the exophthalmos. This is sometimes due to a thickening of the bone in this region or rarely to the fact that the bone has been perforated by the tumor which continues to grow in the temporal fossa. A homonymous notch in the visual fields may result, or uncinat seizures, from compression of the temporal lobes. Finally the symptoms of increased intracranial pressure inevitably supervene.

The *diagnosis* must be made from all other causes of unilateral exophthalmos. The fact that in cases of meningioma the protrusion develops very slowly and does not pulsate, of course rules out at once many causes of exophthalmos. Syphilis may cause a similar condition. I have twice seen a unilateral exophthalmos subside rapidly after antiluetic treatment. Tuberculosis and metastatic carcinoma are rare causes. Thrombosis of the cavernous sinus or arteriovenous fistula cannot be confused because of their severe concomitant symptoms. The *principal* differentiation has to be made from tumors back of the eyeball. An orbito-ethmoidal osteoma causes a slowly developing exophthalmos accompanied by persistent frontal headache, sometimes protuberance of the brow, and displaces the eyeball downward and outward. The corresponding eyeball resists attempts to displace it backward. The osteoma may be felt with the finger or seen in the roentgenogram. Tumors of the optic nerve displace the eyeball axially. They usually begin in

youth. The eye becomes blind early with symptoms of optic neuritis followed by atrophy. The mobility of the eye remains good. Sarcoma in the orbit is common at any age, and arises in any relation to the eyeball. The eyeball is not only displaced forward but often pushed aside, especially outward, and its movement impeded. In the roentgenogram an erosion of the bony orbit may be visible. Angiomas in the orbit or in the retro-orbital region within the skull may cause unilateral exophthalmos which does not pulsate. The increased regional vascularity may indicate the correct diagnosis; it increases with crying and straining. There is no bony erosion or thickening. As soon as a bruit develops the eyeball begins to pulsate. A mucocele may develop from the frontal or ethmoidal sinuses. The only symptoms are exophthalmos and its attendant diplopia. Dermoids occasionally arise in the outer part of the orbit but rarely push the eyeball forward. The exophthalmos of xanthomatosis (451) occurs usually in children.

A meningioma of the sphenoidal ridge does not always cause exophthalmos. I will show you now a more complicated case in which there were two large meningeal tumors, one on the sphenoidal ridge and another in the region of the cribriform plate. This woman (CASE XV) of fifty-five has always been well except for an attack of jaundice for which cholecystectomy was done some years ago. She considered herself well and was working steadily as a masseuse until six months before admission, when she began to have headaches and pain in the back of the neck. Systematic questioning, however, elicits the important fact that she has been blind in the left eye for "several years"; she cannot remember exactly how long. Glasses given her by various opticians did not help and the vision was gradually lost. At the age of about fifty she also lost her sense of smell. But it was only in the last six months that she felt at all ill. She then began to have headaches, sometimes in the frontal, again in the occipital region, at times accompanied by sharp pain in the nape of the neck. The headaches became increasingly frequent and in the last two months she became very drowsy, inattentive and untidy. Her memory was poor and her vision began to fail also in the right eye.

She was very drowsy when admitted. It was difficult to keep her attention and her memory was obviously defective. She stated that she was very much ashamed to be so forgetful. The history was obtained mainly from her son. Her general physical condition seemed excellent. There was a complete anosmia. The left optic disc was white and sharply

outlined; this eye was totally blind. The right optic disc was reddened and its outlines hazy but there was no measurable swelling. The left pupil did not react to light but reacted consensually. There was a slight ptosis of the left upper eyelid. The movements of the ocular muscles were free. Visual acuity in the right eye was 0.3+1; the right visual field was generally constricted. There was possibly a slight exophthalmos of the left eye. There was a slight lower facial weakness. The left arm and leg were definitely weaker than the right and there was a tendency toward an extensor plantar reflex on the left side. The tendon reflexes were also more easily obtained on the left side.

Roentgenogram of the skull revealed a thickening and increased density of the left wings of the sphenoid bone, surrounding the left optic canal. The lateral wall and lateral part of the roof of the orbit were involved also and the left anterior clinoid process was tremendously enlarged. Tests for lues were negative on the blood and spinal fluid. A diagnosis was made of meningeal tumor invading the sphenoid ridge on the left side. It was thought that the intracranial tumor must be of considerable size to explain the symptoms, particularly the anosmia. The homolateral pyramidal signs could be explained by compression of the right cerebral peduncle against the tentorium cerebelli.

A low temporo-frontal osteoplastic exploration was made. The spongy and thickened bone was removed including the temporal region, the sphenoidal ridge, the lateral wall of the orbit, and the lateral part of the roof of the orbit. The wound was then closed, and reopened a week later at which time the dura mater was opened. A flattened reddish mass of tumor was found attached to the dura mater in the neighborhood of the superior orbital fissure. The left optic nerve was involved in a mass of bone infiltrated by tumor. There were also several other small nodules about half a centimeter in diameter scattered on the inner surface of the dura mater covering the frontal lobe. These were removed but seemed insufficient to account for the symptoms and the brain remained very tense. Exploration revealed a large tumor beneath the frontal lobe. In order to expose it the prefrontal area was removed. The tumor was then taken out piecemeal. It filled the entire frontal fossa, and was attached firmly to the region of the cribriform plate. The falx cerebri was pushed over to the right and upward by the tumor which extended beyond the midline. The enormous cavity remaining after the extirpation was filled with normal saline solution and the wound was closed.

Her convalescence was stormy. There was a massive edema of the left eyelids and weakness of the right face and arm. For many days she was stuporous and later could not speak, although she understood apparently what was said to her. It is now a month after operation. Anosmia and blindness of the left eye remain but the vision of the right eye is good and she is alert and attentive. But the effect of the lesion of the frontal lobes is still apparent in a tendency to "wisecracking" and a certain loss of social poise. She tells, for example, in a boastful way and with evident relish, of several sexual contacts before her marriage and wants to know whether a venereal infection which she contracted at that time were not really responsible for her condition. The remnant of her difficulty of speech is slight but definite. Ordinary speech is correct but she is unable to repeat complicated phrases such as "National Hospital for Patalyzed and Epileptics." She always balks somewhere in repeating the national anthem although she can sing it and can tell when it is repeated correctly. For half an hour she tried to repeat "Land where my fathets died" pronouncing always "lied" no matter how she approached this line.

Although there was also in this patient a meningioma of the sphenoidal ridge the neurological symptoms were largely due to the tumor in the olfactory groove. The symptomatology of MENINGIOMAS OF THE OLFACTORY REGION is well known (134). From the position of a meningioma of the cribriform region one might surmise that the symptoms would develop in the following order: (1) ipsilateral anosmia from direct involvement of the olfactory bulb; (2) ipsilateral primary optic atrophy by pressure on the optic nerve; (3) complete anosmia because of involvement of the contralateral olfactory bulb; (4) mental symptoms from compression of the frontal lobes of the brain; and (5) contralateral papilledema due to increased intracranial tension. Practically, this chronological development is rarely observed. When the patients are first seen the disease is already far advanced. The anosmia is usually bilateral when first tested. In our climate nasal disorders are so common that a relative anosmia is not rare. Its significance is often obscured also as the result of nasal operations directed against the visual disturbances. Moreover, an anosmia may result from increased intracranial tension alone. It is a symptom to be weighed carefully in the light of the entire clinical picture. Only if it is definitely unilateral and there are no complicating intranasal factors is it a symptom of the greatest importance.

Typically the pressure on the ipsilateral optic nerve results in the clinical syndrome known as retrobulbar neuritis (296). At first there is no alteration to be seen in the optic disc or at most a temporal pallor; exploration of the visual field discloses a central scotoma. Later the pallor spreads to the entire optic nerve-head and the atrophy may progress to complete blindness. It is quite conceivable that in certain cases both optic nerves could be compressed, resulting in a bilateral primary atrophy, or that the direct compression of the optic nerve could occur after the establishment of a choked disc from intracranial hypertension, also that in other instances the tumor might never reach the nerve so that a bilateral choking would result.

Mental symptoms are common, especially in the later stages of the illness, and numerous records have been published in the annals of institutions for the insane of patients afflicted with such tumors who have died there. The most common mental alteration seems to be a simple deterioration terminating in a profound dementia. More rarely there is euphoria contrasting strangely with the deplorable condition of the patient. Symptoms of intracranial tension are late to develop. Even the choking of the optic discs is due more to local congestion than to general increase of pressure. I remember having seen one necropsy at which the convolutions of the frontal lobe were quite flattened and the sulci obliterated, whereas the surface of the rest of the brain appeared quite normal.

The tumor is more or less bilaterally situated just behind the crista galli and, when large, projects backward over the sella turcica involving the optic nerves (Fig. 76). It is firmly adherent to the cribriform region and may erode its way into the ethmoidal cells. The falx cerebri cuts a groove into its upper surface. The surface is covered with small nodules resembling those of a golfball. Its texture is usually very fibrous and avascular.

The *diagnosis* is based largely on the characteristic triad of anosmia, optic atrophy, and mental disturbance, *but should be suspected earlier whenever there is a slowly developing unilateral central scotoma*. It is rarely possible to see in the roentgenogram any alteration of the subjacent bone. Still more rarely some calcification in the tumor may be disclosed. The mental symptoms are not characteristic, but their association with obvious lesions of the olfactory and optic nerves should direct attention to the local character of the causative agent. Confusion with retrobulbar neuritis of toxic origin should not occur in typical cases and, in

those whose ocular alterations are bilateral and obscure, the associated anosmia should aid in the diagnosis. Gliomas of the frontal lobes of the brain rarely cause anosmia or optic atrophy. To do so they must be located on the orbital surface; in this situation they are infrequent. Glioma of the optic chiasm sometimes causes disturbances of vision which are difficult to interpret and might be confused with those due to meningioma of the olfactory groove, but the youth of the patient, the dilatation of the optic foramina, the hypothalamic symptoms, or an associated generalized neurofibromatosis generally suffice to differentiate the former. Cranio-pharyngiomas in adults may cause central scotomas and anosmia, leav-

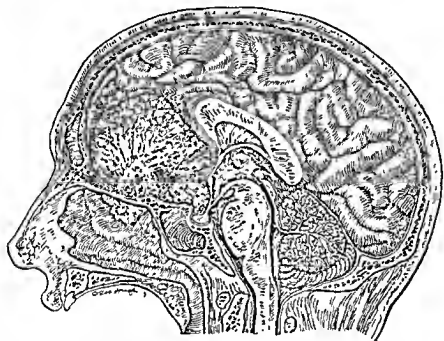


FIG. 76. Median section of the head with meningioma of the cribriform region which has invaded the nasal cavity.

ing the sella turcica intact or very slightly eroded. If suprasellar calcification be absent it may be very difficult to differentiate them from meningiomas of the olfactory groove. However, even in such cases the intensity of the hypophysial or hypothalamic symptoms will usually indicate the correct diagnosis. When a meningioma of the tuberculum sellae has reached a considerable size it may be difficult to differentiate, but of course so long as a bitemporal hemianopia exists confusion

should not occur in spite of a possible anosmia. Because of the marked mental symptoms diagnoses such as senile dementia, senile arteriosclerotic dementia, and taboparesis have been made. Such diagnoses have usually been arrived at when the patient came under observation very late in the course of the disease; they would doubtless not have been made had the patients been observed earlier.

MENINGIOMAS IN THE SUBTENTORIAL FOSSA are rare; arising from the clivus or from the totcular they are very difficult to diagnose. When they arise near the foramina of exit of the cranial nerves they cause characteristic early palsies. In the internal acoustic meatus they may be impossible to differentiate clinically from acoustic neurinomas. I may show you a single example of such a tumor which arose near the entrance of the fifth nerve into the cavum Mecklii (24). In this situation they may explain many so-called atypical trigeminal neuralgias.

This woman (CASE XVI) of sixty-five years had been well until nineteen years ago when she began to have pain in the left side of the face. She described the attacks as "waves" of pain. They lasted thirty to sixty seconds. An injection of alcohol into the fifth nerve was attempted unsuccessfully. Eleven years later an attempt was made elsewhere to section the sensory root by the tempotal route, without success. This attempt was repeated two years later. Numerous injections of alcohol were made in the succeeding years with only partial success.

When admitted to the hospital she was found to be a feeble old woman, almost totally deaf, and speaking almost no English. There was a large depression in the left temporal region. The left masseter and tempotal muscles were paralyzed. The left palpebral fissure was narrow and there was a definite enophthalmos. It was very difficult to examine the patient because of her pain, to which she reacted as to a typical essential neuralgia. There was evidently some diminution of sensory acuity in the left trigeminal area, the details of which could not be established. There was also generalized arteriosclerosis, moderate hypertension, and possibly an old coronary thrombosis, at any rate there was a history of anginal attacks. The old lady insisted that she be operated on, and it was finally decided to cut the nerve by the suboccipital route, because the scars of previous tempotal operations seemed to make success by that route improbable.

Under ether-anesthesia the left suboccipital region was opened. On retracting the cerebellum the petrous vein was found to be much more superficial than usual. It was clipped and divided. The seventh and

the eighth nerves were rapidly identified, but in place of the fifth nerve a mass of grayish-red tissue was seen. This was gradually separated from the petrous pyramid and finally shelled out completely. It was about 1.5 cm. in diameter and firm. The side of the pons was then clearly visible, but no fifth nerve was seen. The oozing was checked by irrigation and the wound closed. That afternoon the patient had a chill and her temperature rose to 39.5° . She then recovered steadily. There was a transitory left facial weakness. She was unsteady on her feet and very weak for a long time and has since been bothered by anginal attacks. Her pain is gone, however, and there is a total anesthesia of the left fifth nerve. It is now several months since the operation and the pain has not recurred.

The only TREATMENT for meningioma in any locality is removal as early as possible, but this is rarely easy to accomplish. The vascularity in the neighborhood may be extreme so that I have known the removal to be balked at nine successive attempts by the excessive bleeding. These tumors may moreover, as we have learned, arise in the neighborhood of the great venous sinuses of the dura mater so that a complete removal necessitates entering these venous channels with resulting profuse hemorrhage. Ligation of the sinuses is difficult and one must be particularly careful not to ligate the superior longitudinal sinus back of the entrance of the superior cerebral veins coming from the central convolutions because a paraplegia may result. The situation of the meningiomas of the olfactory region, sphenoidal ridge, and tuberculum sellae make them particularly difficult to remove; special operative technique is necessary to deal with them (134). If not completely removed the symptoms recur after an interval of months or years. But when a meningioma has been successfully removed the result is usually most gratifying. Since the nervous structures are compressed and not invaded by these tumors, their functions are merely arrested and rapidly recover.

CHAPTER 9

TUMORS OF THE VASCULAR SYSTEM

HEMANGIOBLASTOMA MALFORMATIONS

In 1926 a young Swedish pathologist, Arvid Lindau, was studying cysts of the cerebellum. He noted that some of them had in their walls hemangiomatic nodules instead of the gliomatic tissue he had expected. In scrutinizing the records of the latter cases more closely he found that the hemangiomatic cysts were often associated with a disease of the retina known as angiomas retinac (von Hippel's disease). A study of the cases of this retinal disease disclosed that it was frequently accompanied by symptoms of increased intracranial tension and that in some instances a cyst of the cerebellum had actually been found at necropsy. Lindau immediately concluded that the two lesions were etiologically related and called the pathological complex angiomas of the central nervous system (321). It has since been referred to as *Lindau's disease*. Its discovery is a perfect example of the sort of clinicopathological reasoning which has led to the great syntheses of medicine as we know them. I have seen only one example of the complete syndrome as described by Lindau, but the hemangiomatic tumor in the cerebellar fossa is relatively frequent.

This man (CASE XVII) has such a tumor. He is forty years old, previously well. A year and a half ago he was taken one day suddenly with a severe frontal headache. He has had a headache almost every day since, sometimes very severe, usually transitory in the morning. The headache was relieved by lying flat on the floor; at its worst it was most severe in the frontal region. He was dizzy and it seemed as though his head would burst. Three weeks previous to admission to the hospital a turbinate bone was removed from his nose to relieve the headache. Two days later he became suddenly faint and dizzy and lost consciousness for a few moments. Since that time he could not sit upright without fainting. He noticed also that his tongue felt swollen and numb and that his speech was indistinct.

When admitted to the hospital he lay quietly with contracted brow, evidently in great pain. He would change his position only with the

utmost precaution. He would not move the head on the neck but held it rigid. The optic discs were swollen 5-6 diopters; the visual fields were normal. There was possibly a slight right facial weakness and a definite weakness of the left masseter muscle. The left corneal reflex was absent and slight objective sensory loss over the face could also be demonstrated. The lower jaw deviated to the left when opened. There were some slight nystagmoid movements of the eyes when he looked to the extreme right. There was slight, if any, cerebellar incoördination of the extremities with the usual tests but it was difficult to examine his gait because when placed in the upright position he became dizzy and faint and had to be put back to bed. He stood with his legs far apart and tended to fall backward.

He was thought to have a tumor in the fourth ventricle; the trigeminal anesthesia could be explained by pressure on the spinal fifth tract and the vertigo by involvement of the vestibular nuclei. But many of the above mentioned signs, explicable in retrospect, were not very definite and he was so difficult to examine carefully that it was decided to puncture the ventricles before operating. They were found to be symmetrically dilated. A suboccipital craniectomy was then made and there was disclosed, after removal of the posterior part of the atlas, a red smooth-walled tumor filling the posterior cistern, pushing the tonsils of the cerebellum aside and firmly attached to the dorsal surface of the bulb at the posterior extremity of the fourth ventricle. Large tortuous pulsating bloodvessels could be seen to surround and enter this mass. The removal of a fragment for microscopical study provoked a hemorrhage which was controlled with difficulty. The wound was closed without further attempt to remove the growth. He was drowsy and lethargic for several days, complaining of headache and dizziness, and his optic discs remained swollen. But within a month he began to improve. He was given roentgen radiation over the suboccipital region which has been repeated at intervals since. When discharged he was still unable to stand alone but had no headache. The papilledema had completely subsided. He returns now, two months after the operation, feeling quite well. He has had no dizzy spells and no headaches. His gait is unsteady but he can walk alone, as you see. The weakness of the face and left masseter muscle has disappeared. The left corneal reflex is present. The optic discs are flat but there is some secondary atrophy.

THE ORIGIN OF THESE HEMANGIOBLASTOMAS is from a vascular primordium at the posterior end of the fourth ventricle. In the angle

between cerebellum and bulb, in the third fetal month, there exists a very rich capillary plexus of bloodvessels which for the most part enter into the formation of the choroidal plexus in the roof of the fourth ventricle. A smaller portion forms a vascular tangle at the posterior extremity of the fourth ventricle known as the area postrema. Just in the situation of this latter vascular anlage was our tumor located. This is a very frequent site for such tumors although they may be found over the lateral surfaces of the cerebellar hemispheres or in the spinal cord, where they may possibly arise in relation to similar vascular primordia. It is strange that a tumor which probably arises in a congenital malformation should give symptoms only in adult life, the

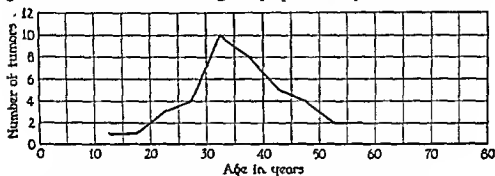


FIG. 77. Age-distribution of hemangioblastomas of cerebellum.

average age of onset of symptoms in these cases being about thirty to thirty-five years (Fig. 77).

The GROSS APPEARANCE of these tumors is well known (Fig. 78). Several have been described (154). They have varied in size from 1 cm. to 5 or 6 cm. in diameter. The tumor is mainly solid but usually contains numerous small cystic and hemorrhagic spaces. Its surface is very red from the contained blood and when injured at operation bleeds profusely. The surface is irregularly nodular, and many large bloodvessels are closely adherent to it. It is attached firmly to the bulb but may be readily dissected loose from the cerebellum. Less commonly such solid tumors may be embedded in the substance of the cerebellum, bulb, or spinal cord. Usually, however, within the nervous tissue they are associated with the formation of a cyst (140). Commonly the cystic cavity is many times the size of the tumor which appears as a reddish or brownish nodule projecting into the lumen of the cyst. The mural nodule may lie in any part of the wall but is usually situated posteriorly. It may even be buried completely in the wall and its presence be dis-

closed only by a discolored dimple (421). The mural tumor is almost always in the cortex cerebelli and connected with the pia mater. The cyst is usually filled with a yellowish or orange-colored fluid which coagulates on standing. Rarely the cystic fluid may be greenish-black from old hemorrhage. The cyst is almost always in one hemisphere or the other; it rarely lies in the midline. The inner wall of the cavity is smooth and glistening. I can show you a patient who suffered from such a cyst.

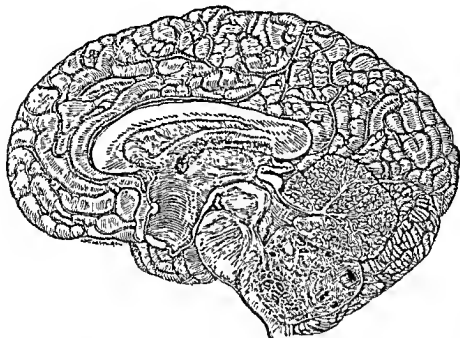


FIG. 78. Median section of the brain with hemangioblastoma of the calamus.

A woman (CASE XVIII) of thirty-seven years, previously well, began about a year before her admission to complain of periodic headaches, in the left occipital region, radiating to the top of the head. At first she could obtain relief from them by taking aspirin but eight months after the onset they became more frequent and severe. She would scream with pain, stagger when attempting to walk and did not seem to know what was going on around her. She saw things double, became dis-oriented and finally comatose.

When admitted to this clinic she was comatose with stertorous respiration and a bloodpressure of 174/108. An intravenous injection

of 50 ccm. of 50 percent glucose roused her quickly. The bloodpressure fell to 108/80; she became very noisy and called for water. Her neck was stiff; it was impossible to flex it anteriorly. The optic discs were swollen 5-6 diopters with numerous hemorrhages far out into the retinae. The right external rectus muscle was completely paralyzed, the left weak. There was no nystagmus. There was a general hypotonicity of all the muscles and the tendon-reflexes were difficult to obtain. She did not cooperate very well for cerebellar tests and we did not attempt to make her walk. The promptness with which she awoke after injection of glucose indicated that she might have a hydrocephalus. But there were no very definite signs of disturbance of the cerebellum. On the other hand the family stated that in the last year her character had changed greatly. She complained that some woman was sticking knives into her head and conceived a bitter hatred of her husband. In the hospital she was very noisy, vituperative, and uncooperative. We could not be sure whether the tumor was in the cerebellum or frontal region and so made an injection of air which showed the lateral ventricles to be symmetrically dilated. The third ventricle seemed normal.

A suboccipital craniectomy was made. In the left cerebellar hemisphere was found a large cyst and within its lateral wall a reddish, very vascular nodule about a centimeter in diameter. This was removed and proved to be a capillary hemangioma. Her condition improved immediately. The choking of the optic discs subsided and she is now quiet and cooperative. The weakness of the left external rectus muscle has disappeared but not of the right. Careful search of her retinae has not revealed any retinal angiomas. Careful inquiry of her family has not revealed illness of any other member which might be interpreted as indicating either an angiomatosis retinae or a cerebellar cyst.

The method of formation of these cysts is uncertain. They may be formed by degeneration in the tumor, since small degenerative cysts are common in the mural nodule. If so, the cavity soon breaks out into the surrounding nervous tissue and is enlarged by transudation from the bloodvessels. The cystic fluid resembles in chemical composition the plasma of the blood, and exerts constant pressure on the nervous tissue which slowly yields to form the cyst.

The MICROSCOPICAL STRUCTURE of these tumors is quite characteristic (139). They are composed essentially of a tangled mass of capillary spaces, which may be empty, but are usually filled with blood. The

cells are usually typical elongated endothelial cells with elongated vesicular nuclei and dense cytoplasm. They are surrounded by a network of strands of reticulin with some collagen in sclerotic areas. Between the capillary tubes there is a certain number of endothelial cells, filled with droplets of fat, called pseudoxanthomatous (Fig. 79). The capillary spaces vary greatly in size; many form veritable caverns. Degenerative changes are widespread. Smaller or larger cystic spaces filled with a coagulum of protein are found. Fatty infiltration is universal. The walls of many capillaries are transformed into a hyalinized mass. Hemorrhages



FIG. 79. Drawing of microscopical preparation of a hemangioblastoma.

are frequent. Reparative processes result in the formation of collagenic scars.

Many variations of the microscopical appearance are formed by predominance of different cellular elements. Typically the tumor is made up of a range of capillary spaces with very little intercellular tissue. However, occasionally the intervascular pseudoxanthomatous cells may proliferate to such an extent that the tumor resembles a hypernephroma or xanthoma. Rarely intervascular cells contain little fat; the tumor then has been diagnosed endothelioma. On the other hand the vascular spaces may be widely dilated so that they dominate

the structure and a cavernous appearance is produced. These variations in structure seem to be of minor importance and may be found in different parts of the same tumor. The tumor has no capsule. The capillary loops seem to invade the cerebellar tissue. The wall of the cyst is composed merely of a slight condensation of the neuroglia.

The relationship of hemangioma of the cerebellum to angiomatosis retinae is definitely established (140). The essential lesion of the latter malady has been shown to be a capillary hemangioma. A few investigators have stated that the tumors in their cases were vascular gliomas. Some of these tumors I have been able to examine and know them to be typical hemangioblastomas. Probably in every case of von Hippel's disease the primary lesion is a hemangioblastoma although later its nature may be obscured by secondary pathological alterations of the eyeball such as proliferative retinitis, detachment of the retina or glaucoma. Not every hemangiomatous cyst of the cerebellum can be shown to be associated with a hemangioma of the retina, but it must not be forgotten that the latter lesion may be discovered only by careful microscopical study. Even so it is probable that either hemangioblastoma of the retina or hemangioblastoma of the cerebellum may occur alone, both being partial manifestations of a larger pathological complex. Their relationship probably is similar to that of acoustic neurinomas and peripheral neurofibromatosis in the pathological complex known as generalized neurofibromatosis.

The essential and most common lesions of Lindau's disease are hemangioblastoma of the retina and of the cerebellum, so that Lindau gave it the name of angiomatosis of the central nervous system. There are, however, other associated pathological alterations elsewhere in the body. Most common seem to be multiple cysts of the pancreas. Rarely there are found also cystic kidney, hypernephromas or tumors of the epididymis. It has been definitely established that the disease is hereditary; it has been followed for three generations in two separate families and seems to depend on the simple dominant inheritance of a single factor, not sex-bound (345). Very few examples of the complete syndrome have been reported but doubtless now that attention has been attracted to the subject they will be more frequently found. The reason for the association of these various pathological alterations is not clear but it is believed to be due to some disturbance of the development of the mesenchyme during the third fetal month of life.

The SYMPTOMS of hemangiomatous cyst do not differ essentially

from those of any other tumor in the cerebellum. The diagnosis of hemangioma of the cerebellum must be made principally from the acoustic neurinoma, the only common tumor in the subtentorial region of adults. The characteristic clinical course of the latter tumor usually enables one to recognize its character. Positive clinical identification of a hemangioma of the cerebellum depends upon the demonstration of an associated hemangioma of the retina (Fig. 80). The essential lesion of angioma of the retina appears as a reddish, rounded elevation usually in the periphery of the retina and often in its lower segment (140). It may be solitary or accompanied by others in various parts of

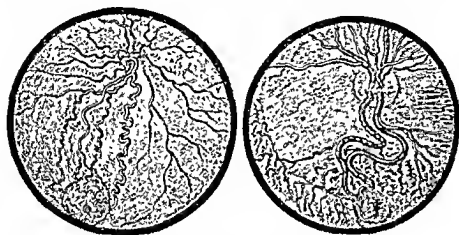


Fig. 80. Hemangiomas of the retina: the one at the left is uncomplicated, the one on the right is complicated by retinitis and detachment of the retina (after Scarlett).

the same or opposite retina. Extending from the optic disc to the hemangioma is a pair of large tortuous bloodvessels. It is difficult to distinguish the artery from the vein by its color, but the artery has often a peculiar beaded contour near the optic disc and in this region may be quite narrow. If more than one angioma exists other similar pairs of vessels will be seen. The retinal lesion is rarely observed in the above simple form. Its essential nature is usually obscured by a secondary retinitis (Coats) which may completely hide the hemangioma. Detachment of the retina, iridocyclitis, glaucoma and other alterations may occur to make the diagnosis difficult.

The TREATMENT of hemangioma of the cerebellum is very satisfactory. It should not be forgotten, however, that simple evacuation of the cyst is not sufficient. If the mural hemangioma is

not sought and removed the cyst will soon refill. The removal of the solid hemangiomas which are attached to the region of the calamus scriptorius is more hazardous. It may be attempted, but respiratory difficulties are apt to occur, and if the tumor is not too large one should probably be content in most cases with a decompression and subsequent roentgen radiation.

In addition to the hemangioendotheliomas of Lindau's type there occur in the brain so-called RACEMOSE ANGIOMAS which, although not properly angiomas, are yet called by this name and often cause clinical syndromes which are with difficulty distinguished from those of true neoplasms. Vascular malformations of this nature in the brain are of three types—arterial, venous, and capillary (139). It is known that multiple telangiectases in the skin and mucous membranes have a tendency to occur in families (365). In certain instances they have been associated with multiple telangiectases in the central nervous system and in other internal organs, particularly the liver. As many as thirty or more such lesions may be scattered about throughout the brain, spinal cord, and retina. Most often, however, these small vascular malformations occur singly and have an especial predilection for the upper part of the pons.

The *capillary telangiectases* of the central nervous system are small tangles of bloodvessels varying in diameter from a few millimeters to 2 or 3 centimeters. The bloodvessels also vary from the size of an ordinary capillary to huge cavernous spaces. In the latter case the lesion is usually described as a cavernoma. The walls of the vessels consist of a few strands of collagenic tissue, often hyalinized and sometimes calcified; rarely is there any muscular coat. Between the vessels is a variable amount of sclerotic and degenerated cerebral tissue, especially in the margin of the nodule; nearer the center, the walls of the vessels may be in contact. A variable amount of hemosiderin is usually found in the neighborhood. These telangiectases cause no characteristic symptoms and their presence can only be inferred from concomitant telangiectatic lesions in the skin.

Occasionally at operation or necropsy there are disclosed over the surface of the cerebral hemispheres *venous malformations* looking like tangles of coiled soaks. They may occur over any part of the hemisphere but are most common in the distribution of the middle cerebral veins. The lesion appears to be superficial but experience has shown that it usually extends deeply into the cerebral substance, often reaching the ventricular wall. In the latter case there is sometimes a central core of

smaller veins from which the larger ones radiate as in a caput medusae. At operation the vessels have the dark-blue color of veins and are often exceedingly thin-walled. They pulsate as a mass with the brain, but no pulsation of their contents is visible unless there is an arteriovenous communication within the lesion. Such was the appearance of the cortex of this next patient.

He is a young man (CASE XIX) of thirty-five years, previously well except for an ichthyosis vulgaris, who was taken suddenly two years before his admission to the hospital with a sensation of tightening and spasm in the right hand. It lasted but a few seconds, but similar attacks occurred every few weeks afterward, beginning always in the arm, whence the sensation crept up the arm and sometimes down the right side. Usually the right leg was not involved but he sometimes staggered as if drunk. During the attacks the right arm was flexed and adducted and afterward he was always very sleepy. He never had any headache. He began to be very nervous and irritable, and an increasing weakness of the right arm and leg caused him to seek medical aid.

When admitted to the hospital he seemed a sturdy, healthy man. There was an evident ichthyosis of the forearms and legs. There was a slight tremor of the head at rest. There was a definite blurring of the margins of the optic discs but no measurable elevation. Visual acuity and visual fields were normal. There seemed to be some diminution of cutaneous sensibility over the right side of the face and diminished acuity of hearing with the right ear, of middle-ear type although there was no history of otitis media and the right ear-drum was normal. There was a fine tremor of the outstretched hands. The tendon-reflexes on the right side of the body were generally brisker, but there was no clonus at the ankle and the plantar reflex was normal. Muscular strength was definitely diminished on the right side. The patient stuttered badly but insisted also that lately he had difficulty in remembering the names of objects. Comprehension of written and spoken language seemed normal.

On the left side of the face was an extensive but pale reddish-violet relangiectasis (Fig. 81). All over the head, but loudest over the left temporal region, was to be heard a swishing noise synchronous with the beat of the heart. The heart itself was of normal size; the blood-pressure was 124/80. It seemed very probable that there was an angiomatous malformation of the left cerebral cortex and an exploration was advised.

An osteoplastic operation was made in the left temporoparietal region. The scalp and bone bled profusely and as soon as the dura mater was opened there could be seen (Fig. 82) a large number of hugely dilated veins and arteries. One large vein more than three millimeters in diameter followed the course of the great anastomotic vein but all over the exposed cortex the vessels were greatly dilated. In the temporal and parietal regions were tangled masses of small ves-



FIG. 81. Patients with facial nevi and concomitant cerebral nevi. At the left, CASE XIX; at the right CASE XX.

sels and deep in the temporal region were more tortuous vessels which could not be exposed because they seemed to be adherent to the under surface of the dura mater. The veins did not pulsate individually but the whole cortex seemed to heave with each beat of the heart. The dura mater itself was extremely vascular in the temporal region. The wound was carefully closed and, contrary to the usual custom, drained. The patient recovered promptly. The decompressed area is soft and pulsates markedly. The bruit is still clearly audible in the left temporal region. A transitory aphasia has now disappeared. He is being given roentgen treatments at the present time and has had no epileptic attacks since his operation two weeks ago. He says that his right arm and leg have now recovered their strength.

The bloodvessels of these lesions have the microscopical structure of veins, but their walls are very thin and often no muscular cells can be identified. In other regions leiomyomatous nodules are present and also nodular hypertrophy of the intima (82). There is no elastica interna. Hyaline degeneration of the vascular walls is frequent and occasionally calcification occurs. Some of the vessels are thrombosed. Hemorrhages are common. Between the vessels there are islands of sclerotic and compressed cerebral tissue, often calcified.

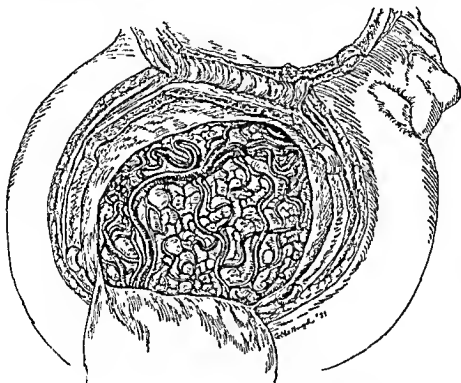


FIG. 82. Appearance of the cerebral cortex at operation on CASE XIX.

The almost constant symptom of the venous angiomas is epilepsy which usually begins in young adult life and is often focal in type because of the situation of the lesion. But the attacks may begin with a generalized convulsion and any type of aura occurs depending on the location of the angioma. There is rarely any choking of the optic discs but occasionally a unilateral exophthalmos and slight bulging of the corresponding temporal region. Still more rarely occur contralateral hemipareses of the type associated with birth-palsies. Some mental retardation is also not uncommon.

The diagnosis of venous angiomas is sometimes made easier by a concomitant congenital nevus of the face on the same side as the lesion, as in the patient I have just shown you; in these cases there is usually present also a vascular anomaly of the leptomeninges. In the absence of a tell-tale facial nevus the diagnosis may be aided by the calcification of the adjacent cortex which casts parallel tortuous shadows on the roentgenogram. Such a roentgenogram I can show you. It was taken of this young girl (CASE XX) fifteen years of age who complains of attacks of unconsciousness. The first one occurred at the age of fourteen and was soon succeeded by others. The last one occurred

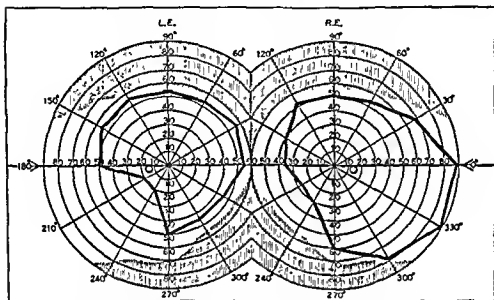


Fig. 83. Visual fields from CASE XX.

at the dinner-table. Her head turned to the left, her eyes rolled and she was unconscious for a moment or so. There seems to have been no other muscular movements. She was previously well but mentally not very bright. Her brother remarked that she always had an "inferiority complex." She had an operation for strabismus when four or five years of age. As a child she had no "spells," walked and talked at the normal time. There was nothing to suggest an injury at birth. She had never been seriously ill.

She seems a normal girl for her age. Only the left eye does not converge well and the right does not rotate outward well. The visual acuity is 0.5—1 in the right eye and 0.1 in the left. The optic discs are normal. In the visual fields, however, is found a homonymous defect in

the left lower quadrants (Fig. 83) and a roentgenogram of the skull discloses a shadow in the right occipital region with the parallel tortuous lines typical of the calcification associated with these lesions (Fig. 84). Over the right forehead is a large bluish-red nevus (Fig. 81).

Arterial malformations differ from the venous ones in the active pulsation of the individual coils of vessels. Sometimes in a large thin-walled vessel a stream of arterial blood may be seen to pour from an



FIG. 84. Scheme of roentgenogram from CASE XX showing typical calcification in parallel tortuous lines associated with a cerebral angioma of the occipital region. Compare Plate XIII.

anastomosis. These lesions have obviously been always arterial or have become arterialized by formation of an arteriovenous fistula (153). *The result of the fistula is the development of an intracranial bruit, rarely absent, and usually audible to the patient although he may be unaware of it until it is called to his attention. The bruit can be heard by auscultating the head with a stethoscope. It is usually loudest over the mastoid process and along the great vessels in the neck but should be listened for also over the temporal, supra-orbital, and occipital ar-*

teries. In one patient I could hear it plainly over one occipital artery although it was inaudible to the patient himself and had been reported absent by a number of physicians. The bruit has a rhythmic accentuation synchronous with the beat of the heart, and usually has a swishing sound, but in advanced cases there may be an almost continuous roar. It is usually reduced or obliterated by compression of one or both carotid arteries.

The formation of an arteriovenous communication also results sooner or later in alterations of the extracranial vascularity. Large pulsating vessels may develop in the scalp, originating in large emissary communications with the intracranial cavity. The carotid arteries of one or both sides may be enlarged and pulsate exaggeratedly in the neck. There may even be a secondary cardiac hypertrophy. Similar vascular alterations, of course, follow the establishment of an arteriovenous fistula anywhere in the body. In contrast to the venous angiomas some papilledema is rarely absent and usually most evident on the side of the lesion. Rarely the retinal bloodvessels may take part in the angiomatous process. More frequent is a unilateral exophthalmos which rarely pulsates although the bruit may be plainly audible over the bulb of the eye.

One of the most frequent symptoms, as of the venous angiomas, is epilepsy of focal type. It is in no way specific and in those rare cases in which the angioma occurs over the cerebellum it may be absent. After the attacks there is often a transitory paralysis or other defect of nervous function, depending on the location of the lesion, such as transient aphasia or hemianopia. Headaches and vomiting rarely occur. *The clinical evolution of the lesion is usually terminated by an intracranial hemorrhage as in the following case.*

A young man (CASE XXI) thirty-nine years of age entered a hospital in deep coma with a temperature of 40° , a pulse-rate of 96 and bloodpressure of 140. His pupils were dilated and did not react to light. His urine was normal but a lumbar puncture obtained very bloody cerebrospinal fluid under high tension. A few hours later he died without regaining consciousness. The only history it was possible to obtain was that he had always been well until two weeks previously when he suddenly had a severe headache and lost consciousness for a few moments. A few days later a similar attack occurred and two days before admission to the hospital a third attack from which he never recovered.

A complete examination was made postmortem which disclosed a

slight insufficiency of the mitral valve. The heart weighed 330 grams. There was a confluent pneumonia of both lungs but nothing else of importance was found outside of the brain. The brain can be seen to be covered with blood, especially over the base. The subarachnoid space is everywhere filled with it. The left temporal lobe is distinctly larger than the right and a firm mass can be felt in its tip. The bloodvessels over this lobe are greatly dilated. Section of the brain shows the left

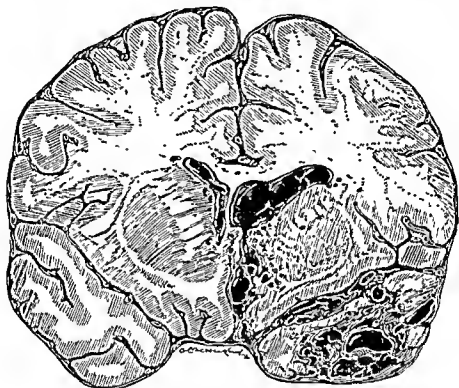


FIG. 85. Cross section of the brain from CASE XXI with venous angioma in the tip of the left temporal lobe.

temporal lobe to be the seat of a tangled mass of bloodvessels 3 cm. in diameter (Fig. 85), and extending 4 cm. backward from its tip. The middle cerebral artery on this side is 4 mm. in diameter. The left optic thalamus is partially destroyed by hemorrhage which has broken through into the left lateral ventricle. All the ventricles are filled with clotted blood.

One must in these malformations distinguish the essential vascular anomaly and the entering and draining bloodvessels (153). It is

quite possible in the patient which I showed you a while ago that on the cortex we saw only the veins draining a deeper-lying arteriovenous fistula which had caused the bruit. The entering artery, usually the middle cerebral, is dilated, sometimes sacculated, and tortuous. The draining veins are hugely dilated and often very thin-walled (Fig. 86). They usually lie on the surface of the brain although in one instance, at least, the exit was through a markedly dilated great cerebral vein (of Galen). The extent of the involvement of the veins seems to depend on the number and size of the vessels of the essential lesion and on the size and directness of the arteriovenous communication.

When examined postmortem it is difficult to distinguish an arteriovenous angioma from a venous angioma since the actively motile characteristics of the former are lost. These anomalies usually lie in the area of the middle cerebral artery; less commonly the anterior cerebral is involved and rarely the cerebellar arteries. They are essentially superficial lesions since the ramifications of the cerebral arteries begin in the pia mater, but usually an entire vascular area is involved, both trunk and branches, so that the entire lesion has the shape of a cone, the base being on the surface and the apex reaching even the ventricular wall. Sometimes the vascular mass is supplied by more than one major artery.

Microscopically the essential lesion is found to be a tangle of blood-vessels of varying caliber separated by more or less sclerotic and often calcified cerebral tissue. The walls of the vessels vary greatly in thickness and structure. Some can be recognized as arteries by the well-developed elastica interna. Others have only scattered strands of elastin throughout the wall. Very few vessels have a longitudinal muscular coat; in many there are no muscular cells, in others leiomyomatous nodules are found. The intima is often proliferated and transformed into fibrous tissue. In the same vessel the wall in one region may be very thick and in another consist of only a few strands of collagenic tissue. Hyaline degeneration of the vascular walls is frequent and calcification is not rare. Many of the vessels are thrombosed and evidences of old hemorrhages are usually present. Aneurysmal out-pocketing of the vessels is very frequent.

The DIAGNOSIS of an arterial angioma is based on the combination of a cranial bruit and increased extracranial vascularity. A cranial bruit may occasionally be normally heard in infants. Contrary to the usual opinion it is rarely audible in cases of intracranial aneurysm, unless an arteriovenous fistula has been formed. Rarely a bruit may be heard over a vascular meningioma. In general, however, an intracranial bruit, es-

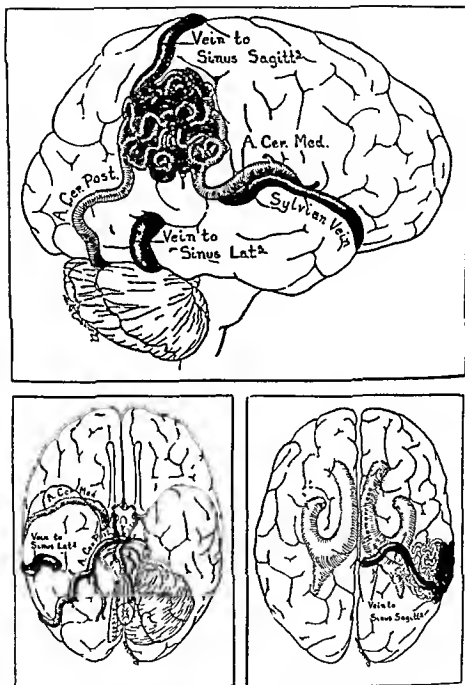


FIG. 86. Diagrammatic representation of an arterial angioma with its chief entering and draining vessels (from Cushing and Bailey). Compare Plate XIV.

pecially if concomitant with epileptic attacks and dilatation of the extracranial bloodvessels, is indicative of an arterial angioma. The unilateral exophthalmos may make one suspect a meningioma of the sphenoidal ridge, but the absence of erosion or thickening of the sphenoidal wings should correct this impression and the positive symptoms noted above lead to the correct diagnosis. In rare instances a preoperative diagnosis may be established from the roentgen examination, which discloses the characteristic parallel tortuous lines of calcification occurring with venous angiomas. If the foregoing symptoms are absent the diagnosis may still be established by arteriography (cf. Plate XIV).

THE ORIGIN OF THESE VASCULAR MALFORMATIONS is to be sought in the young embryo where the angioblasts differentiate directly from the mesenchyme, not only of the area vasculosa of the yolk-sac but also in the embryo itself (414). They form first solid clumps of cells which unite into bands or cords and later plexuses. These cells have a different cytoplasm from the original mesenchymal cells, and tend to form solid masses which appear like a syncytium and to put out sprouts which join similar masses. In the interior of the cords and clumps of angioblasts a lumen appears by a process of cytolysis, the peripheral cells becoming less granular and flattening to form endothelium. The endothelial cells can give rise to other endothelium or angioblasts.

The vascular plexus first forms around the forebrain and midbrain and by sprouting spreads over the wall of the entire brain. At first it is a germinal bed of endothelium but later it slowly differentiates into feeding and draining channels and a capillary bed (460). The capillary sheet hugs closely the surface of the brain while the more superficial parts of the plexus form larger channels. Intermediate loops of the plexus maintain the communication between the larger channels and the capillary bed. By differentiation of the meninges and skull the primitive vascular system is stratified into the three layers of superficial, dural, and pial vessels. The cleavage begins over the base and spreads upward to the vertex where it is long incomplete, and even in the adult the emissary vessels maintain the embryonic anastomoses. The cerebral system of bloodvessels later undergoes a long series of readjustments in which older channels are obstructed and newer ones take their places as the form of the brain makes its remarkable transformations. Finally when the adult relationships are fairly well established the histological changes occur which differentiate the vascular channels into adult arteries, veins, and capillaries.

It can be seen, therefore, that the vascular system adapts itself constantly to its changing environment and any disturbance of the orderly evolution of the structures of the head may result in anomalous development of the vascular system. On this basis it is easy to understand the formation of the vascular anomalies we have just described. In case an insult affects the vascular primordium before its cleavage into superficial, dural, and pial systems we can readily understand the simultaneous production of superimposed vascular anomalies of scalp, dura mater and pia mater as the abnormal vascular bed is cleft into three layers.

The TREATMENT of racemose angiomas is not very satisfactory. When one is disclosed at operation it would best be left strictly alone and later subjected to roentgen radiation. If one is reasonably certain of the diagnosis such lesions may be radiated before a craniotomy is undertaken, sometimes with prompt amelioration of symptoms. In at least one case such radiation so reduced the vascularity that it was possible at a secondary operation successfully to extirpate the central lesion. Rarely such a lesion may be removed by primary attack (383).

CHAPTER 10

TUMORS OF THE INTERSTITIAL TISSUES

HISTOGENESIS

CLASSIFICATION

Ependymoma: Syndrome of the Fourth Ventricle

The last decades of the nineteenth century were occupied with the detailed study of the structure of tumors, the separation and classification of the different forms, and with writing the life-history of malignant neoplasms. With the twentieth century began an era of experimental study by the aid of transplantation into animals, culture of tissue, and other methods looking toward the discovery of the cause of cancer. But it is usually true that any new method of attack on a problem finds many disciples who abandon the older methods before they have given their full harvest. This was certainly true in the case of tumors of the brain. Until very recently practically all tumors of the brain were called gliomas. Virchow seems first in 1867 to have maintained that they arise from the interstitial tissue of the brain. Golgi, in 1875, demonstrated in them the characteristic star-shaped neuroglial cells of the white matter of the brain and distinguished soft and hard varieties. It was recognized that some were benign while others grew very rapidly. But the analysis did not go far beyond these simple findings. The diagnosis was usually based on the demonstration of neuroglial fibrils by the method of Weigert or one of its modifications. Because the neoplastic cells of the malignant ones are often spindle-shaped these tumors were somewhat confused with the spindle-celled tumors of the connective tissue and so came to be known as gliosarcomas. Later there was a tendency to liken the neoplastic cells to embryonic neuroglial cells and the term spongioblastoma was used.

In general the term glioma is not sufficiently inclusive to be appropriate for all tumors developing from the encephalon. An occasional sarcoma or hemangioendothelioma develops from the connective tissues of the brain. The papillomas are also encephalic tumors, developing from the choroid plexuses of which the epithelium represents the entire thickness of the neural tube. Occasional tumors also contain neurones (medulloblastoma, ganglioneuroma) but they are usually

composed mainly of cells of interstitial origin so that they may be grouped with the gliomas without doing any great violence to their structure. I will, therefore, neglect the rarer tumors (cf. Chap. 17) and confine my attention to the tumors of the interstitial tissue, including some which may contain also neurones. A nomenclature and classification of these tumors has recently been elaborated (45) which brings some order into their myriad structural variations and enables one from the microscopical structure, in a certain measure, to predict the behavior of the growth. This classification reposes upon the finding that in tumors of the brain the neoplastic cells have a tendency to reproduce the structure of certain embryonic forms found during the development of the central nervous system. Its understanding demands a knowledge of the MICROSCOPICAL STRUCTURE AND HISTOGENESIS OF THE BRAIN, especially since recently the normal microscopical structure of the brain has been better understood and new categories of cells isolated (51).

There is no need to enter into details concerning the structure of the *neurones*. The appearance of the large motor cells in the anterior central region of the cerebral cortex and in the anterior horns of the spinal cord is very familiar. But it might be well to recall that many of the nervous cells are not of this pyramidal type. The sixth layer of the cerebral cortex is composed mainly of cells having a fusiform shape and in the granular layers are innumerable cells which have very little cytoplasm at all and in which the tigroid substance is very scanty. All of these cells, however, may be recognized by their vesicular spherical nuclei in which the nucleoli are very prominent. But there are other cells, for example in the granular layer of the cerebellum, in which even the vesicular nucleus is lacking and whose nervous nature is recognizable only by the reaction of their unmyelinated processes to impregnation with silver. In the peripheral ganglia occur other neurones of much different structure from those of the brain. It should not be expected, therefore, that neurones in tumors will look like pyramidal cells.

The *interstitial cells* (Fig. 87) are less well known since the recent advances in our knowledge of them have just begun to penetrate into textbooks. Two general groups are now recognized, known as the neuroglia and microglia. The neuroglia is composed largely of the classical astrocytes of which there are two forms, the protoplasmic and the fibrillary. The fibrillary astrocytes are found mostly in the white substance of the brain. They are typically star-shaped with very little cytoplasm around the oval nuclei and many long branching processes. Fibrils

are differentiated in the processes and may be sharply and differentially stained. There is always one stouter process which is attached by a trumpet-shaped extremity to the wall of a bloodvessel. In the cytoplasm are also numerous fuchsinophile granules called gliosomes which are found far out along the processes. The processes are narrow and their cytoplasm dense. The nuclei are oval with delicate and fairly evenly scattered granules of chromatin. The protoplasmic astrocytes are found mainly in the gray matter of the cortex. Their processes, although

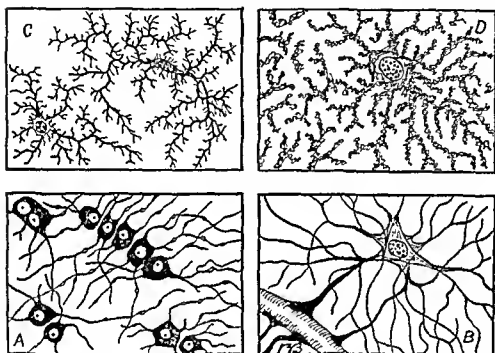


FIG. 87. Normal interstitial cells of the brain. A—oligodendroglia; B—fibrillary astrocyte; C—microglia; D—protoplasmic astrocytes (after Hortega).

equally numerous, are thicker and more irregular. There is a stout vascular process. No fibrils are differentiated but the peripheral cytoplasm stains somewhat more heavily. In both types of astrocytes are found gliosomes, a reticular apparatus (of Golgi), and a centrosome usually in the form of a single large granule at the base of the vascular process. A rarer type is the perivascular neutoglia cell (of Andriezen) of which the cell-body lies on the bloodvessel, a vascular process being absent.

Besides the *astrocytes* two other types of cells have been recently isolated in the interstitial tissues, the *oligodendroglia* and *microglia*

(51). Of these the former is closely allied to the astrocytes, while the latter seems to be of quite different nature. They were relatively disregarded until recently because of the difficulty of staining their processes. The oligodendroglia are small cells found principally along the long fiber tracts but occur also as perineuronal and perivascular satellites. They have more or less polygonal bodies, from the corners of which extend delicate branched processes very difficult to demonstrate. They have gliosomes, rudimentary reticular apparatus, and centrosome usually in the form of a diplosome. There is no vascular process. Many forms may be seen which appear to be transitions to astrocytes. The nuclei are round, smaller than the nuclei of the astrocytes, and have a much heavier reticulum of chromatin. The microglia (of Hortega) differs widely from the astrocytes and oligodendroglia. These cells have no gliosomes and no reticular apparatus, at least none has ever been demonstrated. The processes are covered with lateral spines. Usually two stouter processes extend from the two poles of the nucleus. These cells are scattered widely over the central nervous system and behave quite differently from the neuroglia, becoming scavengers whenever there is any destructive process going on.

The earlier stages of the *histogenesis of the brain* are familiar to you from your courses in embryology. The central nervous system begins as an invagination along the median dorsal surface of the embryo, forming a medullary groove. The folds of this groove close to form a long tube called the medullary tube. From the dilated anterior end of the tube the brain differentiates. The details of the finer histogenesis have recently been supplemented by the results of new methods of impregnation (45). At first the medullary tube consists of a columnar epithelium, the medullary epithelium, but mitoses occur near the inner border, and these dividing cells are called germinal cells. They are the precursors certainly of the nervous cells of the brain. Their transformation may be followed in all its stages (Fig. 88). First there is an enlargement of the nucleus which becomes spherical and vesicular. The chromatinic network largely disappears or at least is rarefied and one, or sometimes two, very distinct nucleoli become apparent. The centrosome is extruded to the periphery of the cytoplasm or disappears completely. The cytoplasm at one or both opposite poles of the nucleus becomes denser and develops an affinity for silver. At this stage the cell is already recognizable as a neuroblast and, since it has no processes, is called an apolar neuroblast. From the denser area of the cytoplasm—

the fibrillogenous or argentophilic zone (of Held)—a process arises which becomes the axis-cylinder. At this stage the cell is called a unipolar neuroblast and by the development of other processes destined to be dendrites it becomes a bipolar or multipolar neuroblast. Finally with the accumulation in its cytoplasm of the tigroid substance and the formation of a myelin-sheath around the axis-cylinder it is transformed into an adult neurone.

By the proliferation of the neuroblasts and other cells between

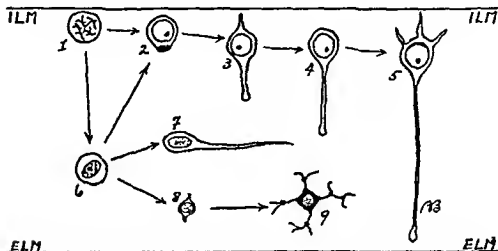


FIG. 88. Scheme of evolution of the germinal cells. ILM—internal limiting membrane of the brain; ELM—external limiting membrane of the brain. 1—germinal cell; 2—apolar neuroblast; 3—bipolar neuroblast; 4—unipolar neuroblast; 5—multipolar neuroblast; 6—medulloblast; 7—unipolar spongioblast; 8—oligodendroblast; 9—oligodendroglia.

them, the remaining cells of the medullary epithelium become separated and elongated. At their inner, or ventricular, ends they develop cilia with a small granule called a blepharoplast at the base of each. In this stage they are known as primitive spongioblasts. Some of them continue on into adult life with little modification, for example in the ventral raphe of the spinal cord. Elsewhere, with the increasing distance between the ventricular and pial surfaces the connection with the pia mater is lost. The cilia also disappear, except in a few places such as the floor of the fourth ventricle, and the blepharoplasts migrate into the interior of the cytoplasm. The cells are then called ependymal spongioblasts. Many of the ordinary ependymal cells lining the ventricles of the brain have entirely lost their pial processes. Such is the evolution of those pseudo-epithelial cells whose cellular bodies remain along

the ventricle to form the ependyma (Fig. 89). Others of the primitive spongioblasts lose their connection with the ventricular surface (Fig. 90). The cytoplasm between the nucleus and the ventricle is drawn out to a long process. In this stage the cell is called a bipolar spongioblast. The connection with the ventricle is later lost and the body of the cell becomes piriform; it is now called a unipolar spongioblast. After the ingrowth of bloodvessels into the central nervous system whatever the tails come into contact with the vessels an attachment occurs. The distal part of the tail atrophies whereas the proximal portion becomes very stout. At this stage the vascular process dominates the appearance of

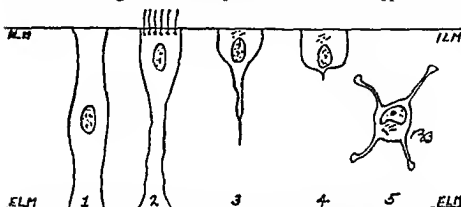


Fig. 89. Scheme of evolution of the ependymal cells. ILM—internal limiting membrane of the brain; ELM—external limiting membrane. 1—medullary epithelium; 2—primitive spongioblast; 3—ependymal spongioblast; 4—ependymal cell; 5—pineal cell.

the cell, which begins to put out feeble processes from its other extremity. It is now known as an astroblast. By the continued extension of the non-vascular processes it is transformed into an adult astrocyte.

It does not seem possible, however, that the tremendous numbers of astrocytes in the brain can be accounted for by the process outlined in the preceding paragraph. Though difficult to prove, in an attempt to explain numerous facts of the normal structure and development of the brain it has been found necessary to suppose that the germinal cells give rise not only to neuroblasts but also to more embryonic undifferentiated cells which we may call medulloblasts. Migrating and dividing in an undifferentiated state they finally form either neuroblasts, spongioblasts, or oligodendroglia. This hypothesis seems best to explain the structure of the deeper regions of the brain, where astrocytes and oligodendroglia lie in juxtaposition along the long fiber-tracts.

The origin of the microglia is not definitely established. It is supposed to come from the mesenchyme and certainly when it is earliest identifiable it lies in close proximity to the deepest extensions of the pia-arachnoid, for example near the velum interpositum. From these regions it is supposed to migrate throughout the central nervous system. The histological activity of the microglia is quite different from that of the other interstitial cells and more comparable with that of the phagocytes of mesenchymal origin. We may, therefore, accept the hypothesis of its origin from the mesenchyme until it is disproved.

Finally we might mention that in the pineal body the medullary epithelium follows another evolution and develops into a special type

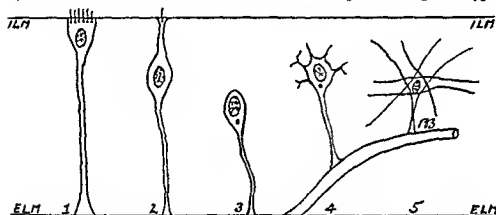


FIG. 90. Scheme of evolution of the astrocytes. ILM—internal limiting membrane of the brain; ELM—external limiting membrane. 1—primitive spongioblast; 2—bipolar spongioblast; 3—unipolar spongioblast; 4—astroblast; 5—astrocyte.

of cell, known as the parenchyma of the pineal body (280). The histogenesis of the brain may be recapitulated in a diagram (Fig. 91).

All of these embryonic and adult cells, with the exception of the microglia, may be identified in brain-tumors with greater or less frequency and occasionally tumors are composed predominantly of a single cellular type. Of course, most of them contain several types of cells which at best reproduce only crudely the normal embryonic cells (426). It is necessarily so, since the cellular types which have been isolated represent only transitory phases of a continuous development and, moreover, the tumors are pathological and not normal growths. It is equally understandable, whether we suppose that a tumor arises from an embryonic cell and differentiates or that it arises from an adult cell and "dedifferentiates," that growths composed uniquely of one cellular type should be rare. A tumor composed of spongioblasts, oligodendroglia,

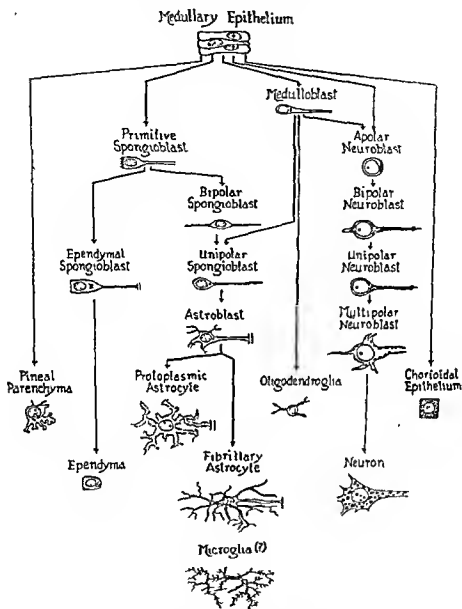


FIG. 91 Scheme to recapitulate histogenesis of brain.

and astrocytes is readily explained on either basis. But a classification is justifiable for didactic purposes. In treatises on pathology, in the chapter on tumors of the connective tissues, one finds described the fibroma, the osteoma, the chondroma, the myxoma, the sarcoma, etc., whereas in

actual experience everyone knows it is sometimes necessary to diagnose osteo-chondro-myxo-fibrosarcoma. Nevertheless purer forms are found and in these cases it is possible to attach a prognostic significance to their structure. In a similar way a classification of brain-tumors is made, based on the structure of the predominant cellular type.

As a matter of fact when one looks long at the kaleidoscopic continuum of brain-tumors certain familial resemblances emerge and when the tumors are grouped in accordance with these resemblances it is evident that in each group a certain cellular type dominates the microscopical appearance. When the clinical histories are correlated with the microscopical structure it is further evident that the various groups have characteristic sites of origin and clinical courses peculiar to themselves (41).

The groups which are most readily distinguished are the following:

- | | |
|-----------------------------|-----------------------|
| 1. Glioblastoma multiforme | 6. Astroblastoma |
| 2. Astrocytoma | 7. Ependymoma |
| 3. Medulloblastoma | 8. Pinealoma |
| 4. Oligodendroglioma | 9. Ganglioneuroma |
| 5. Spongioblastoma (polare) | 10. Neuro-epithelioma |

On histological grounds the astrocytomas may be subdivided into protoplasmic and fibrillary types, the pinealomas into adult and embryonic types, and the ependymomas into adult and spongioblastic types, but there seems little practical advantage in doing so. If now the ten major groups which we have isolated be analyzed clinically we will find that the structural differences are correlated with differences in behavior.

The *glioblastoma multiforme* occurs very frequently. It develops almost exclusively in the cerebral hemispheres of adults (Fig. 120). It grows very rapidly, the average length of the clinical course between the onset of symptoms and the death of the patient being about twelve months. Hemorrhages and degenerations in the tumor are the rule, so that the symptoms often begin or change abruptly. The tumor is composed microscopically of very anaplastic neuroglial cells. Most of the cells are of bipolar, fusiform shape so that the tumor resembles grossly a spindle-celled sarcoma and was formerly described as a gliosarcoma. Many of the cells resemble medulloblasts, unipolar spongioblasts, perivascular cells (of Andriezen), astroblasts, and even small astrocytes. Multinucleated cells are common (Fig. 121) and many mitoses are

found. The cut surface is a kaleidoscopic display of red, yellow, brown, gray, and white. There is no capsule. The multiformity of the histological appearance is due not only to variations in the form of the neoplastic cells but also to the widespread degenerative and reparative changes.

The *astrocytomas* occur anywhere in the brain. They are very slowly-growing indolent tumors. There is a marked tendency for them to undergo a sort of liquefaction causing the formation of large cysts (Figs. 103, 104) practically destroying the tumor, which may persist only as a small mural nodule. These tumors are avascular and hemorrhages into them are rare. In children they are usually in the cerebellum (124), whereas when they lie in the cerebral hemispheres they usually cause symptoms only in adult life. The cut surface is gray and smooth. They may be either soft or very firm. Microscopically they are composed mainly of astrocytes (Fig. 105) either of protoplasmic or fibrillary type. Many are of transitional type. Their time of evolution is very long, sixty-seven months or more.

The *medulloblastoma* is almost exclusively a tumor of the cerebellum of the child (46). It evolves rapidly in fifteen months or less. Usually situated in the middle of the cerebellum it projects into the fourth ventricle (Fig. 96) and has an unusual tendency to invade the meninges and spread widely in the subarachnoid spaces, even to the olfactory bulbs in one direction and to the cauda equina in the other. It is a solid, reddish tumor, very vascular, but hemorrhages and cystic degeneration are uncommon. It often seems grossly to be encapsulated in the cerebellum. Microscopically it is composed mainly of small cells with hyperchromatic nuclei (Fig. 97). The cells have very little cytoplasm. Mitoses are frequent. It is supposed that the neoplastic cells are medulloblasts because in some cases both neuroblasts and spongioblasts may be identified in the tumor. Rarely one of these tumors may be composed so predominantly of neuroblasts as to merit the name of neuroblastoma. Its growth may be readily checked by roentgen-radiation.

The *oligodendroglioma* (43) is almost exclusively a tumor of the cerebral hemispheres of adults. It is very often calcified so that it casts a shadow in the roentgenogram. It grows slowly, the average length of evolution being about sixty-six months. Hemorrhages and cystic degeneration are uncommon. Microscopically it is composed of small round cells with spherical nuclei. The cytoplasm stains so poorly that it often seems to form a halo around the nucleus (Fig. 112). Many of the cells may be impregnated by methods for the oligodendroglia.

The *spongioblastoma* (50) is also an indoleot growth which has a predilection for the brainstem and is especially common (Fig. 125) along the optic tracts (235). Its time of evolution is long, being over forty-six months. It is a grayish, avascular, firm tumor with little tendency to cystic degeoration. It is occasionally calcified. It occurs usually in children and often associated with peripheral manifestations of neurofibromatosis. Microscopically it is composed essentially of bipolar and unipolar spongioblasts (Fig. 129).

The *astroblastomas* (44) are a rather poorly defined group of tumors which occur in the cerebral hemispheres of adults. They have many of the characteristics of the glioblastoma multiforme but grow more slowly; their average clinical course extends over a period of more than twenty-eight months. Microscopically they are composed mainly of astroblasts. Transitional forms are found to glioblastoma multiforme on the one hand and astrocytoma on the other. There is a characteristic overgrowth of connective tissue around the numerous bloodvessels.

The *ependymomas* (22) occur along the walls of the ventricles, especially in the fourth ventricle (Fig. 93). They often give symptoms in childhood. They are slowly growing tumors, practically innocuous if it were not for their unfavorable situation. Two varieties are distinguished, the ependymoma and the ependymblastoma. Both are indoleot growths which cause symptoms mainly by blocking the circulation of cerebrospinal fluid. Microscopically they are composed of ependymal cells or ependymblasts (Fig. 94) with characteristic blepharoplasts in the cytoplasm. The ependymblastoma is the most frequent glioma of the spinal cord (299).

The *pinealomas* (276), as their name implies, develop from the pineal body. They give rise to characteristic symptoms because of their situation. Their structure imitates that of the pineal body at some stage of its development. In the adult type there is a characteristic association of pineal cells and lymphoid tissue (Fig. 134).

The *ganglioneuroma* (110) is a very rare tumor which may occur in the brain but is much more common in the peripheral nervous system. It is characterized microscopically by the presence of numerous neoplastic nerve-cells.

The *neuro-epithelioma* is also a very rare tumor in the brain and spinal cord; it is especially frequent in the retina (235) which is, after all, a part of the brain. The striking microscopical feature is the presence of canals surrounded by primitive spongioblasts to form rosettes.

From these brief characterizations it is evident that *each type of glioma is a distinct entity with its own idiosyncrasies* which it is important to recognize. Any attempt to describe "glioma" as an entity only leads to confusion. If now we place these tumors on our scheme of histogenesis (Fig. 92), in accordance with the predominant cellular type, and compare the result with a table of the average survival-time

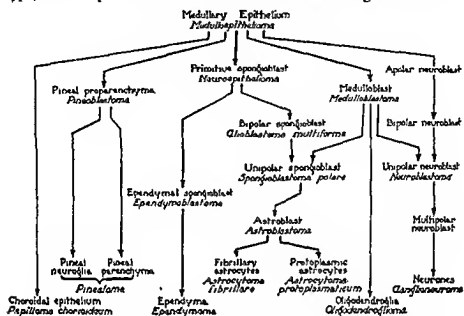


FIG. 92. Scheme to relate types of gliomas according to the predominant cellular constitution of each group.

characteristic of each group of tumors it will be seen that *in general the gliomas composed of cells resembling those of the early stages of histogenesis tend to develop more rapidly*. The average survival-times in months are as follows:

1. Medulloblastoma	15
2. Neuro-epithelioma	—
3. Glioblastoma multiforme	12
4. Pinealoma	18
5. Ependymoma	25+
6. Astroblastoma	28+
7. Spongioblastoma (polare)	46+
8. Oligodendroglioma	66+
9. Ganglioneuroma	—
10. Astrocytoma	76+

Although the neuro-epitheliomas and ganglioneuromas are too rare in the brain for any figures to be significant we know that the neuro-epithelioma of the retina is a very malignant tumor and that the ganglioneuromas of the peripheral ganglia are benign. The survival-times of the pinealomas and ependymomas are shortened because of their unfavorable location in the brain. The malignancy of the ependymal tumors is about the same whether they are composed of ependymal cells or ependymal spongioblasts. For statistical purposes I have, therefore, grouped the ependymoblastomas and ependymomas, which I previously distinguished histologically, together. For the same reason the rare pinealoma of spongioblastic type (pineoblastoma) has been grouped with the pinealomas of adult type. The medullo-epitheliomas, neuroblastomas and other rare types have been ignored. Taking all these things into account it is evident that *the microscopical structure of a brain-tumor is important for prognosis.*

The fact that in these tumors embryonic cells may be found should not be interpreted in the sense of the Cohnheim-Ribbert hypothesis. There is some evidence which indicates that the medulloblastoma may arise from embryonic rests in the cerebellum but for the other types such evidence is almost entirely lacking. There are even indications that the glioblastoma multiforme may arise by dedifferentiation of protoplasmic astrocytes. Moreover, there is no more reason to suppose that every glioma arises in the same way and from the same causes than there is to suppose a common etiology for all tumors. We have already learned that modern developments in the study of cancer have led pathologists to insist on the possibility of multiple etiological factors. But inability to explain the origin of gliomas does not need to hinder us from classifying them tentatively and studying their behavior.

If from a long series of gliomas of the brain verified at necropsy or operation we list all those which may be classified under the ten major groups we have distinguished, the result is as follows:

A. Verified at operation by cystic fluid alone	59
B. Excluded because differential study impossible	64
C. Unclassifiable and rare types	67
D. Classified according to the above scheme	378
Neuro-epithelioma	1
Medulloblastoma	55
Pinealoma	8
Ependymoma	16

Glioblastoma multiforme	117
Spongioblastoma (polare)	12
Astroblastoma	20
Astrocytoma	136
Oligodendroglioma	12
Ganglioneuroma	1
Total	568

Of the large group in which the nature of the tumor was verified at operation by removing characteristic yellow clotting fluid from a cystic cavity the vast majority would probably prove to be either glioblastoma multiforme or astrocytoma. If necropsies could be obtained from these cases and they were then included in the classified list the relative numbers of these two types would in all probability be changed but little; most probably the percentage of astrocytomas would be somewhat increased. One should remark also the number of unclassifiable tumors. In many instances the amount of material removed at operation was insufficient, too necrotic, or removed in a manner to make a microscopical study unreliable, but there still remains a goodly percentage (11.8 per cent) of rare, atypical, transitional, or mixed forms which cannot be fitted into our classification.

A glance at the classified list now shows that 54.2 percent fall into three large groups—the astrocytomas, the glioblastomas, and the medulloblastomas. The last two are formed of rapidly growing tumors which kill quickly, while the first is composed of indolent relatively benign tumors. A study of the whole group indicates that approximately 47 percent (composed of ependymomas, spongioblastomas, astrocytomas, oligodendrogliomas, and ganglioneuromas) are relatively benign tumors with a good prognosis provided that they do not block the circulation of the cerebrospinal fluid. The general impression that the prognosis of gliomas is hopeless—an impression gained largely from the glioblastoma multiforme—is not, therefore, confirmed by careful analysis.

I will try to give clear and detailed descriptions of the more frequent groups of gliomas, and we have time now to begin with the small but interesting group of the ependymomas. I have here a brain containing such a tumor (Fig. 93). It was obtained at necropsy from a child (CASE XXII) of sixteen months who was well until six weeks before admission to the hospital, when he began to vomit persistently. A week later it

was noted that the boy squinted. He had begun to walk only two months previously; with the onset of his illness he ceased to try to walk and remained in bed. He became gradually dull, his head enlarged and there were twitchings of all his extremities.

When admitted the child was emaciated, stuporous, and sucking his fingers constantly. The head was obviously enlarged (51.5 cm. in circumference) and gave a hollow sound when percussed. It was retracted and totated to the left and held stiffly in this position by rigid contraction of the cervical muscles. The child seemed to be blind although the optic discs were only slightly swollen. The pupils were dilated and did not react to light. There was an internal squint of the left eye. Both eyes wandered incoördinately and did not follow lights. There was a slight right facial weakness. The child moved his left extremities much more than the right. The tone of the right extremities seemed greater and there was on that side an extensor plantar reflex. There were rapid myoclonic twitchings of all the extremities perhaps mote on the left side. The child would not coöperate at all with the examiner. His temperature varied from 37° to 37.5°.

The stiffness of the neck indicated that the tumor lay in the cerebellar fossa but there was a fairly definite right spastic hemiplegia. The history of his illness was not sufficiently detailed to be of much aid in locating the lesion. We know that in children the vast majority of intracranial tumors are situated in the subtentorial region but for infants this rule does not hold good (520). Since the outlook was not very bright it was decided to make a ventriculogram first. It revealed a widely dilated ventricular system except for the fourth ventricle which was not visualized. Although the air was immediately removed from the ventricles the pulse became very irregular, respirations were shallow and irregular, and a hyperthermia developed from which he died after a few hours.

At necropsy there was found a large tumor, 5 cm. in length by 4 cm. in breadth, within the fourth ventricle. It was visible externally between the vermis of the cerebellum and the bulh, and extended down into the foramen magnum. The relations of the tumor are best seen on median section of the brain (Fig. 93). The inferior surface is flat and attached in its middle portion to the floor of the fourth ventricle. Its anterior extremity projects into the aqueduct and its inferior extremity downward over the posterior surface of the bulh beyond the calamus scriptorius. Its upper surface indents deeply the cerebellum from which

it is readily separated. The anterior medullary velum is distinct from the tumor, the posterior cannot be identified. The cut surface of the growth is grayish-red in color with a few hemorrhagic spots. The bulb is very much flattened by the tumor and the ventricles widely dilated.

The SYMPTOMS OF SUCH TUMORS WITHIN THE FOURTH VENTRICLE are readily understood (71). They cause early and violent headaches coming on in paroxysms associated with stiffness of the neck and pain which may radiate to the shoulders. The muscles of the neck may be

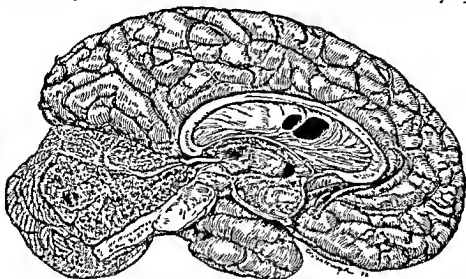


FIG. 93. Median section of brain CASE XXII with endependymoma of fourth ventricle.

tender when palpated and obviously tensely contracted. The head is held very cautiously in the position which the patient has found most comfortable, usually slightly flexed but often retracted (456). Any attempt to displace the head from the optimal position is resisted by the patient who knows by experience that any movement is apt to start a violent headache. Moreover, a sudden movement may produce even more serious results such as vomiting, vertigo, syncope, apnea, or involuntary urination. The headache is caused by blocking of the circulation of the cerebrospinal fluid but the more serious symptoms are due to compression of the medullary centers by the tumor which often projects upward into the aqueduct and downward into the foramen magnum. Various visceral disturbances are provoked by these tumors, probably from irritation of vagal nuclei; often there is vesical tenesmus or difficulty in starting micturition (260). Pains in the epigastrium or pre-

cordial region may cause errors of diagnosis. The vomiting and the urinary troubles may precede the symptoms of increased intracranial tension and when they do so are very suggestive of tumor in the fourth ventricle.

Unless prompt relief is obtained from operation the condition of patients with tumors of the fourth ventricle is soon greatly aggravated. The intracranial tension rapidly increases. The patient becomes stuporous, vomits repeatedly, and the optic discs become rapidly choked with numerous hemorrhages. Attacks occur during which the head is retracted, the back hyperextended, the arms extended and pronated, the legs extended and adducted, the pulse irregular, respirations of the Cheyne-Stokes variety, temperature elevated, and consciousness clouded (218). These so-called cerebellar fits are due to compression of the bulbar centers (492) and one may observe alternating vasodilatation and vasoconstriction, bradycardia alternating with tachycardia, dyspnea, polyuria, profuse sweating, and dilatation of the pupils. At first the attacks may be short but later longer and more severe until one ends in the death of the patient. The fatal outcome has often been hastened at this stage by an ill-advised lumbar puncture.

In addition varied symptoms are present of irritation or compression of the cranial nerves in the cerebellar fossa or of their nuclei, the sensory afferent tracts, or of the pyramidal system. Most constant, however, are cerebellar disturbances predominating in the lower extremities and forming a group which we will discuss later (p. 240) as the syndrome of the vermis. Very frequent also is a general hypotonicity with abolition of the tendon-reflexes probably produced by compression of the vestibular nuclei.

Of course the symptoms I have enumerated are in no way characteristic of ependymomas in general, but the fourth ventricle is the most frequent site of these tumors and when there they cause symptoms similar to those I have just described. Ependymomas occur near the ventricular walls anywhere in the brain, often in the lateral cerebral ventricles. In the latter situation they are frequently calcified and, since they are practically the only calcified tumors in this location in children, the fact is of some diagnostic significance (191). The ependymomas are also usually fairly sharply circumscribed from the surrounding brain, with the exception of the ventricular wall, which makes them easier to remove. They may contain small cystic cavities but rarely large cysts. They are relatively tough and avascular growths.

Microscopically the ependymomas are characterized by the radiation of their cells around small vascular channels (Fig. 94). They may be divided into two groups on the basis of the shape of the neoplastic cells, although there seems no practical advantage in doing so. In one group the cells are polygonal or slightly elongated, with considerable cytoplasm, forming a mosaic. The cellular boundaries are distinct and those cells around the vessels are the most elongated. In the other group the cells are still more elongated, with stout processes which may extend for some distance in the tissue but end finally on the wall of a vascu-

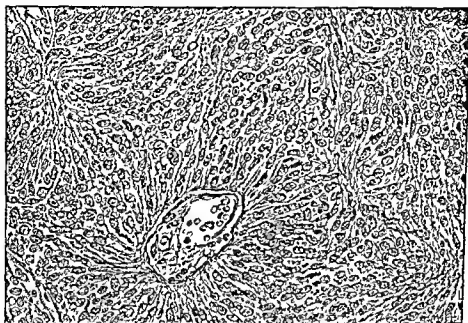


FIG. 94. Drawing of a microscopical preparation of an ependymoma.

lar channel. The cells of the latter group have been likened to ependymal spongioblasts; those of the former group resemble the cells of the medullary vela. Within the cytoplasm of nearly any of the neoplastic cells can be found a group of granules or short rods which stain like the blepharoplasts of the normal ependymal cells.

Such ependymal tumors would be relatively benign growths were it not for their site of origin which makes it easy for them to block the circulation of the cerebrospinal fluid. Some patients have survived for many years, after a decompressive operation has relieved the obstruction, although the tumor has not been removed. When attached in the floor of the fourth ventricle it is inadvisable to attempt their removal.

CHAPTER 11

MEDULLOBLASTOMA

SYNDROME OF THE VERMIS CEREBELLI

In 1925, I isolated a type of glioma which occurs chiefly in the center of the cerebellum of children for which I suggested the name *medulloblastoma*. A preliminary study was published in collaboration with Cushing (46), who has recently made a much more complete survey of the material (136). I will show you this morning a child with typical symptoms, and the brain of another which demonstrates particularly well the peculiarities of structure of this tumor.

This delicate child (CASE XXIII), eight years old, began eighteen months ago to vomit on arising in the morning, usually before breakfast. Before the vomiting she complained of headache. She was irritable and listless during the day and slept poorly at night. She remained at school for three months but had difficulty with her lessons. Her headaches then ceased but she continued listless and vomited her food frequently. The school-physician found that her gait was very unsteady, that she tended to fall backward and that the optic discs were swollen.

She was admitted to the hospital six months after the onset of vomiting. She was very pale and listless. The optic discs were elevated 6-7 diopters with many fresh hemorrhages. Her visual acuity was 0.8—3 in the right eye and 0.8—4 in the left. The visual fields were slightly and concentrically contracted. There was little or no nystagmus; at times a few feeble jerks on looking to the extreme right or left. There seemed to be a slight weakness of the right side of the face and the right corneal reflex was less active. The tendon-reflexes were all greatly diminished. There was a marked relaxation of the musculature of all the extremities, but practically no asynergy of the extremities of cerebellar type. She stood with difficulty by spreading her feet widely apart and her gait was reeling with a tendency to fall backward. The head was enlarged and a "cracked-pot" sound was elicited by percussing the head. The neck was stiff and any attempt to flex the head on the chest caused the patient to cry out with pain. Roentgenogram of the head showed the sutures to be widely separated (cf. Plate III). A diagnosis was made of tumor of the vermis of the cerebellum.

A suboccipital exploration was made through a cross-bow incision. When the dura mater was opened a grayish tumor could be seen between the tonsils of the cerebellum extending down into the spinal canal. The arch of the atlas was removed before the lower end of the tumor could be exposed. The tumor extended upward into the fourth ventricle underneath the vermis which was split sagittally to expose the lesion. As much as would come away readily was then removed by suction. The wound was carefully closed, leaving the dura mater open. Microscopical examination proved the tumor to be a rapidly growing glioma of the type known as a medulloblastoma. The child recovered promptly and was discharged two weeks later at which time she could walk alone but her gait was still somewhat unsteady. The suboccipital region was not tense and she had ceased vomiting. The choking of the optic discs had subsided to two diopters. There was still a marked hypotonicity of all the extremities.

Energetic roentgentherapy directed toward the entire central nervous system was begun. She continued to improve rapidly. A month later she walked and ran normally; could walk a line or hop on either foot without falling. She no longer vomited and gained in weight. There had been no reduction in visual acuity. The nasal margins of the discs were still elevated about 0.5 diopter. The pupils were widely dilated and reacted sluggishly to light. The reflexes were active and the hypotonicity of the extremities much diminished. She was quite well all summer but returned within three months with the suboccipital region bulging and some unsteadiness of gait. There was no swelling of the optic discs. More roentgeno-radiation was given. She returned to school and did well in her school-work. Three months later she was examined again. At this time she was feeling well; the suboccipital region was bulging and tense but there was no headache or vomiting. The optic discs were not swollen. The principal change was in the knee-jerks which were very hyperactive. Roentgen-radiation was again given. Two months later she was quite well, running and playing like a normal child, and the swelling of the suboccipital region was much less.

She returns to the hospital now complaining that for the last month she has been troubled by pains down the backs of both legs. The suboccipital region is bulging and tense, and she occasionally vomits. The knee-jerks are brisk but the ankle-jerks are not obtained. There is no swelling of the optic discs. No sensory loss can be found in the lower extremities, but I fear that the tumor has spread down the spinal cord.

You can imagine what is happening after you have examined this specimen; it is the brain and spinal cord from another child who developed a similar tumor.

The surface of the brain is very smooth. Not only are the convolutions flattened but the sulci are obliterated by a grayish mass of tissue which extends upward in each lateral fissure and spreads out finger-like over the hemispheres (Fig. 95). Over the base of the brain this tissue obliterates all landmarks and can be traced forward around the rostrum of the corpus callosum between the hemispheres and backwards around the pons to the cerebellum. When the brain is cut sagittally the tissue is seen

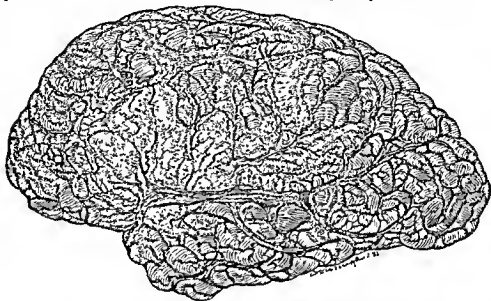


FIG. 95. Lateral surface of the cerebral hemisphere from CASE XXIV.
The tumor has spread along the cerebrospinal pathways.

to coalesce with a large mass occupying the central part of the cerebellum and filling the fourth ventricle but not adherent to its floor. There is a marked dilatation of the other ventricles. It is evident that the tumor of the cerebellum has invaded the subarachnoid space and spread along its main channels, not only forward but also downward, because examination of the spinal cord discloses the same grayish tissue extending especially over the dorsal surface as far as the cauda equina where there are several nodules a centimeter and more in diameter.

The child (CASE XXIV) from whom these specimens were taken at necropsy was three and a half years old. He began, three months before admission to the hospital, to vomit, usually in the morning before break-

fast. He would vomit suddenly and without warning. He did not seem sick and went on playing afterward. A month later the vomiting became more frequent. He was not ill otherwise, did not complain of headache, and walked and ran normally. Various pediatricians were consulted who made gastric studies but could find no cause for the vomiting. Finally he began to vomit constantly, was unable to retain food, and became very weak. When he fell into a snoror another physician was called who found that the optic discs were swollen and sent him to this clinic. During his entire illness he never complained of headache.

When admitted he was comatose and the pulse rate was 50. The neck was stiff. A "cracked-pot" sound was elicited when the head was percussed. The optic discs were elevated but were difficult to measure because of lack of cooperation. All of the extremities were very hypotonic. There was a bilateral extensor plantar reflex. Roentgenogram of the head showed the sutures of the cranium to be separated, and the sella turcica normal with no calcification above it.

In spite of the absence of much cerebellar symptomatology it was determined to make a suboccipital operation. A large, soft, reddish-gray tumor was found in the vermis; it extended downward into the spinal canal and around the bulb. There was a separate nodule on the dorsal surface of the left hemisphere of the cerebellum. It was obviously impossible to remove the tumor and since the child had stopped breathing several times the operation was terminated as a decompression and the wound closed as rapidly as possible. The temperature rose to 39.8° and the pulse rate to 160. His condition was precarious for several days. The palate was paretic and he regurgitated food through the nose so that he had to be fed with a nasal tube. He vomited a great deal and coughed with a brassy sound as though there were a paralysis of the recurrent laryngeal nerve. Fluids were administered intravenously and roentgen-radiation was begun and continued in small doses at frequent intervals over the cerebellum and entire spinal canal. He began definitely to improve about two weeks after the operation, vomited less and began swallowing food well. Two weeks later he was discharged. At this time he had ceased coughing, was swallowing food normally, vomited rarely, and was very alert mentally. There was a nystagmus only when he was turned. All of the extremities were hypotonic. The optic discs were not swollen but slightly atrophic. He was still very weak and could not stand alone.

His condition remained unchanged for nearly a month; then he had

an attack of twitching of his right arm, leg and face, during which he could not talk. He rapidly developed a right hemiparesis, had difficulty in swallowing, and frequent twitching of the right side of the face. On the following day there was a generalized convulsion. The lateral ventricle was punctured and the cerebrospinal fluid was found under no tension. He grew rapidly weaker and died within a few hours. The brain and spinal cord which we have just examined were removed one hour post-mortem.

These medulloblastomas almost invariably develop in children of an average age of ten to eleven years (136), in the midline of the cerebellum just over the fourth ventricle. Rarely a tumor of similar structure is found in the cerebral hemisphere. The gross appearance of these tumors is usually reddish gray. They may be invisible from the outside of the cerebellum, but usually they reach the surface between the tonsils. The appearance of the lesion from the suboccipital surface is of most interest because it is from this aspect that the surgeon sees it at operation. The most common appearance is a fullness of the vermis with herniation of the tonsils into the spinal canal, sometimes as far as the axis. When the tonsils are dislocated upward there can be seen the inferior extremity of the tumor in the fourth ventricle. It projects downward in the form of a small nubbin, somewhat constricted from the main body of the growth. When this inferior extension is not visible after separation of the tonsils its presence may still be betrayed by a fullness of the vermis, and it can be exposed by dividing the vermis sagittally. More rarely the vermis may be transformed into tumor, which is then visible as soon as the dura mater is opened. The tumor is soft and, although it has few large vessels, abundantly supplied with blood mainly from the inferior cerebellar arteries. It can be easily sucked out but the oozing of the blood from the surface exposed is difficult to check because of the absence of large vessels and the softness of the neoplastic tissue. Rarely is there enough connective tissue to give a firm consistency to the growth.

Another peculiarity of the medulloblastoma aids in recognizing it by its GROSS APPEARANCE. *It is of all gliomas the one most apt to invade and spread in the leptomeninges (46).* One may see reddish-gray areas of varying sizes scattered over the suboccipital surface of the cerebellum. They are raised only a couple of millimeters but conceal the folia and vessels beneath. At necropsy the full extent of this leptomeningeal invasion is sometimes surprising as we have seen. The tumor may be followed along the pathways of the cerebrospinal fluid over the basilar sur-

face of the cerebellum and pons into the interpeduncular cistern then along the middle cerebral vessels up the lateral fissures whence it spreads out over the lateral surfaces of the cerebral hemispheres. It passes also anteriorly around the infundibulum onto the median surfaces of the frontal lobes. Extending up the great cerebral fissure (of Bichat) above the tentorium cerebelli it reaches the ambient cistern and spreads over the tentorial and medial surfaces of the occipital lobes. In the spinal

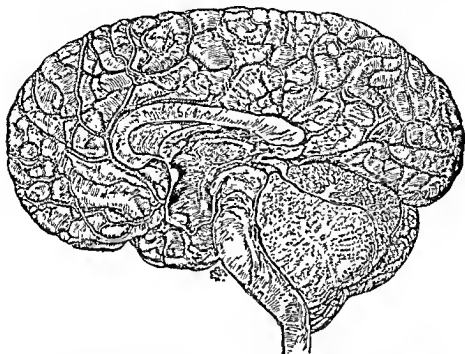


FIG. 96. Median section of brain with medulloblastoma in typical location.

canal it lies mostly on the dorsal surface of the cord, either as small discs or as a continuous sheet. In the cauda equina it takes the form of nodules among the nerves. The extent of spread varies in different cases but some leptomeningeal invasion is rarely absent.

The internal relationships of the tumor are best seen by median sagittal section. It is then found to be centrally situated in the cerebellum (Fig. 96). Its cut surface is finely granular, reddish-gray in color, of fairly uniform appearance and consistency. Cysts, hematomas, and degenerated areas are rare. The anterior vermis is pushed forcibly upward and compressed against the tentorium. The posterior vermis may be completely invaded and destroyed; usually, however, it also is greatly

thinned and distended. The tumor fills the fourth ventricle and compresses the bulb but is rarely adherent to it. There is also often a posterior extension down into the spinal canal. The tonsils of the cerebellum are compressed and forced downward into the spinal canal alongside the spinal cord and tumor. Occasionally fragments of the tumor may be found implanted in the infundibulum of the third ventricle or even rarely along the walls of the lateral ventricles. There is always an internal hydrocephalus of the third and lateral cerebral ventricles. The cortex cerebri is thinned and the convolutions flattened.

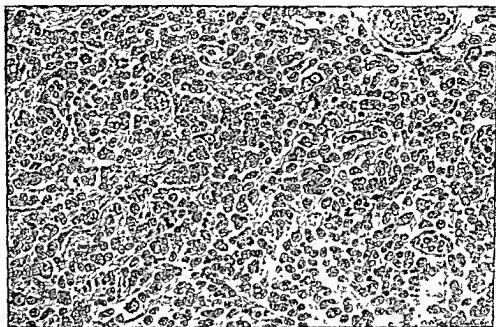


FIG. 97. Drawing of microscopical preparation of a medulloblastoma.

The MICROSCOPICAL STRUCTURE of the medulloblastoma is quite characteristic in most cases (46). It is a very cellular tumor. Its cells are closely packed together. They have very little cytoplasm. The nuclei are oval, with heavy chromatinic network resembling that of carcinomatous cells. Mitotic figures are numerous (Fig. 97). When the teased unstained tissue is examined the neoplastic cells are mostly round but some pyriform cells are found. In fixed preparations the cytoplasm lies mostly in formless strands among the nuclei but often the cells appear elongated, like carrots, with the nuclei at the larger ends. The nuclei have a tendency to be grouped, leaving clear spaces filled with the strands of

cytoplasm. When such a clear area is surrounded by a ring of nuclei the whole formation is known as a pseudorosette. Small thin-walled vascular sinuses are numerous. The connective tissue is usually confined to their walls but there is a variable tendency toward the formation of a stroma which is rarely of sufficient extent to give any firmness to the tumor. The nuclei of the stroma are readily distinguished from those of the neoplastic cells; they are elongated, often with wrinkled nuclear membranes and much less chromatin.

The portion of the tumor which invades the leptomeninx contains much more connective tissue, doubtless because the strands of leptomeningeal tissue form a sort of stroma. This excess of connective tissue has led many pathologists to describe these tumors erroneously as sarcomas and the diffuse spread in the leptomeninx as "sarcomatosis of the meninges."

Closer examination will reveal other types of nuclei. Many are oval and differ from the usual nuclei only in that the chromatinic network is much more delicate. By appropriate methods of staining it can be shown that these nuclei belong to spongioblasts in various stages of differentiation. Still other nuclei are spherical, vesicular and very large. They have prominent nucleoli and very little chromatin and can be shown to belong to neuroblasts in all stages of development. Many of them are apolar with only a fibrillogenous zone (of Held) visible, but usually they are in the unipolar or multipolar stage. It is rare that they contain tigroid bodies. Because both spongioblasts and neuroblasts differentiate in these tumors we may suppose that most of the cells are perhaps bivalent and in an earlier stage of development. To the indifferent or undifferentiated formative cells of the nervous system I have given the name medulloblasts, hence the term medulloblastoma. It is often difficult to find neuroblasts, but I have seen in the cerebellum of a child such a tumor with great numbers of neuroblasts. Rapidly-growing tumors of very similar structure are found also in the retina (retinoblastomas) and in the sympathetic nervous system (sympathicoblastomas).

The usual **COURSE OF THE SYMPTOMS** is somewhat as follows (136): A child about ten years of age begins to complain of headache on arising in the morning, and vomits. He is listless and does his school-work poorly. He holds his neck stiffly and is dizzy. He complains perhaps that he does not see well. He is taken to the school-physician who finds very little in the way of physical signs, diagnoses a gastrointestinal disorder, prescribes a cathartic and soon the child is much better. But

after a few weeks the symptoms return, although headache is now a minor complaint. It is noted, however, that the child stumbles and falls readily and that the head is enlarging rapidly. The diagnosis is sometimes made at this stage of the disease but in a surprisingly large percentage of cases the child continues to be treated for a supposed gastrointestinal disorder or tuberculous meningitis. Meanwhile the child loses weight from the continued vomiting, becomes more and more disequibrated until he is unable to walk and the vision rapidly fails. Finally, the last stage is usually ushered in by attacks in which the child stiffens in an opisthotonoid position with the extremities rigidly in extension and respirations labored. These attacks occur with increasing frequency, and in such an attack respiration ceases and the child dies, some six or eight months after the onset. It is often very difficult to obtain an exact chronological order of development of the symptoms. In fact the parents will often deny symptoms which have long been apparent to the neighbors. However, from the study of a considerable series of cases it seems that headache, vomiting, and staggering gait are most apt to usher in the illness. In very young children enlargement of the head may be the first sign noted.

The headache is rarely severe and may be transitorily present only in the early weeks of the illness. In some patients headache is denied. On the contrary some stiffness and discomfort in the back of the neck is almost constant. The head is often held stiffly in an unnatural position because of the pain. The mildness and transitoriness of the headaches is undoubtedly due to the young age of these patients, which allows them to decompress themselves by separation of the cranial sutures, thus compensating for the increasing hydrocephalus. The vomiting is an almost constant and very early symptom. It is often abrupt, projectile and without nausea. It often occurs in the absence of headache so that it seems to be due to local pressure on the bulb. It occurs at any time but especially on arising in the morning. It has no relation to the taking of food; a child who has vomited his breakfast may be fed immediately afterward and retain the food. The unsteadiness of gait is always present. In the early stages of the disease it is noted only that the child stumbles and falls readily but later he may be completely unable to walk. Other symptoms frequently complained of are difficulty in vision (usually found to be due to squint), loss of weight and mental change—usually listlessness, inattention, and irritability. *Less common symptoms are slurred speech, incontinence of urine, and dizziness.*

Examination of such a child in a fairly advanced stage of the disease shows the outstanding feature of the clinical picture to be difficulty in walking. When the child is placed on his feet he spreads them far apart and sways widely with a constant tendency to fall over backward. He is unable to stand on either foot or to walk a line. When he tries to walk the feet are spread apart, he reels drunkenly and ends by falling backward. The unsteadiness is not increased notably by closing the eyes. The trouble in maintaining the equilibrium is in striking contrast with the slight evidences of ataxia of the extremities when the patient is lying in bed. Nystagmus is usually absent; rarely a prominent sign. The upper extremities usually show little, if any, incoördination by the ordinary tests; even the movements of the lower extremities are often surprisingly steady but usually show more or less dysmetria, asynergia, and tremor. The muscles of the extremities in the early stages are very relaxed; the tendon-reflexes feeble or difficult to elicit. Later the reflexes may be exaggerated with ankle-clonus and extensor plantar reflexes. The head is invariably enlarged. Percussion of the head causes a peculiar hollow sound, due to separation of the cranial sutures, which is known as the "cracked-pot" or Macewen's sign. The enlargement of the head is evidence of internal hydrocephalus.

The neck is held stiffly and any sudden displacement of the head is apt to cause pain. The patient usually resists flexion of the head on the chest but occasionally retroflexion causes most discomfort. In later stages come attacks in which the head is forcibly retracted, the back arched, and the extremities rigidly extended. These are known as cerebellar fits (of Hughlings Jackson). During these attacks the patient perspires profusely, the pulse and respiration are irregular, and consciousness is either lost or the patient is in a semiconscious, dazed condition. The optic discs are usually swollen but the swelling is less than one would suppose from the severity of the patient's condition. This is doubtless due to the separation of the cranial sutures which reduces the intracranial tension. Secondary atrophy of the optic nerves is usually present but rarely severe. The visual fields are constricted and the blind-spots enlarged. Paresis of one or both sixth nerves is common. There may be difficulty in upward conjugate deviation of the eyes.

It should not be forgotten also that actual symptoms of compression of the spinal cord may be produced by the extension of the tumor to the spinal canal. In these cases one finds girdle-pains, sensory loss in the extremities and spasticity. These symptoms and signs occur late in the course of the disease.

Any attempt to understand the peculiar distribution of the neurological disturbances of these patients reveals to us immediately that the cerebellum is still less understood than the cerebrum. Analysis of its functions, in the way we have used for the cerebrum, has been disappointing. In the intact animal the cerebellar cortex is largely, if not entirely, inexcitable in the sense of giving localized muscular responses. The major part of the cortex is supplied by three arteries which anastomose with each other so abundantly that no syndromes have been noted which can be correlated with occlusion of any artery to the cerebellar cortex. The study of wounds received in the World War added little to our knowledge. Moreover, the cortex of the cerebellum has such a uniform structure that cyto-architectonic studies give no clues to differentiation of function. In these circumstances studies of comparative anatomy and physiology have thrown most light on this complicated and obscure structure.

Many studies have been made of the COMPARATIVE ANATOMY OF THE CEREBELLUM (173). In the lowest of vertebrates, the Cyclostomes, the most rudimentary form of cerebellum may be found. In *Petromyzon* it arises just back of the bilobed rectum opticum by fusion of the tubercula acustica to form a median bridge of tissue arching over the anterior extremity of the fourth ventricle. In all vertebrates this position in close proximity to the nuclear mass for the eighth and lateral-line nerves, the so-called octavolateral area, is maintained. The chief afferent paths come from this area but the cerebellum receives other fibers from the roof of the midbrain and from the hypothalamus. Its neurons resemble those of the octavolateral area. In its lateral border is a group of large cells whose axons form a cerebellotegmental bundle, some of which decussate under the nuclei of the third nerves to form a sort of rudimentary brachium conjunctivum. The cerebellum in these animals is clearly dominated by vestibular and lateral-line connections. The presence of spinocerebellar connections has not been definitely proved. This primitive octavolateral part of the cerebellum can be traced throughout the vertebrate phylum.

In those animals living on land the lateral-line system has disappeared and the octavolateral part comes to be dominated by its vestibular connections. In mammals it is overshadowed by the tremendous development of new mechanisms but it is worthy of note that in those mammals which have returned to water, for example the whales, it is relatively much larger than in land-living mammals. In the simpler amphibia, for

example *Necturus*, (254) the cerebellum has a twofold origin. By the proliferation of numerous nuclei in the neural tube there comes to be formed a widened area with a thin roof known in all vertebrates as the fourth ventricle. The point of widest lateral extent of this ventricle is called the lateral recess. Caudal to the lateral recess lies the octavolateral area and its rostral end thickens and differentiates into the auricular lobe of the amphibian cerebellum. With the loss of lateral-line fibers in adult frogs it is dominated by vestibular fibers and is clearly the precursor of the floccular region of the mammalian cerebellum. But the upper border of the lateral recess, which extends across the posterior border of the roof of the midbrain to the opposite side, differentiates under the impulsion of optic and somesthetic fibers from the midbrain and also of fibers of spinal origin. This median portion of the cerebellar

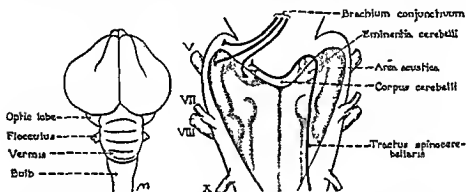


FIG. 98. Schemes of cerebellum in (a) birds and (b) *necturus* (after Herrick).

primordium was destined to a considerable development under the impulsion of its spinocerebellar connections as locomotion on land became more developed. It is the precursor of the vermis of mammals (Fig. 98).

The vermis may be conveniently studied in birds (78) for their cerebellum consists essentially of a median sagittal disc, very thick in the middle, and two lateral auricles (Fig. 98). The latter are intimately connected with the vestibular nuclei and correspond clearly with the octavolateral portions of the amphibian cerebellum or the flocculi of mammals. The median disc just as clearly suggests the mammalian vermis and is similarly divided transversely by sulci which have been homologized with those of the mammalian cerebellum. The avian cerebellum has an inferior and superior peduncle but no middle peduncle. The spinocerebellar tracts are the same as in mammals and end in a similar manner in

the cortex. There are two pairs of subcortical nuclei, medial and lateral. The former send their fibers, mostly crossed, to the bulbar tegmentum (Deiter's nucleus especially) and are clearly homologous to the roof-nuclei of mammals. The lateral nuclei send their fibers crossed through the superior peduncles to the red nuclei. The latter correspond only to the magnocellular parts of the red nuclei of man. The lateral nuclei correspond to the nucleus interpositus of mammals (nuclei globosus et emboliformis of man).

With the advent of mammals certain radical changes in cerebellar architecture are initiated. There is a greater and greater development of tissue between the vermis and floccular regions until in man the hemispheres overshadow all else. Parallel with the development of the hemi-

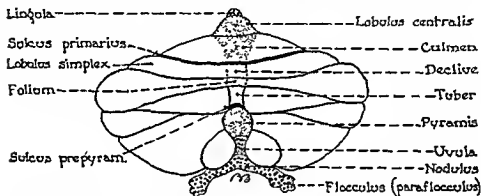


FIG. 99. Scheme showing divisions of mammalian cerebellar cortex into neocerebellum (unshaded), paleocerebellum (dotted), and archicerebellum (circles). Compare with Figure 13.

spheres goes the development of two new structures, among others, the pontine nuclei and the inferior olivary nuclei with their connecting fiber-tracts.

The study of comparative anatomy has, therefore, led to the distinguishing of three fundamental parts of the cerebellum: (1) the very old vestibular (*archicerebellar*) portion, (2) a less old spinal (*paleocerebellar*) portion, and (3) a still newer portion (*neocerebellum*) intimately related, as we shall see, with the cortex cerebri (Fig. 99). Since the tumors we are discussing arise in the vermis above the fourth ventricle they involve principally the first two parts, the afferent and efferent pathways of the neocerebellum being found largely intact. We shall, therefore, confine our attention here to the archicerebellum and paleocerebellum.

The INTERRELATIONSHIPS OF THE VERMIS CEREBELLI are known in some detail. Two important afferent pathways from the spinal cord pass upward to the vermis (Fig. 100). The dorsal spinocerebellar tract (of Flechsig) arises from the nucleus dorsalis (of Clark) and passes upward on the same side of the cord in the lateral funiculus to go via the inferior cerebellar peduncle to the homolateral cortex of the vermis. Some of its fibers may cross in the vermis to the opposite side. More specifically it ends in the lobulus centralis, oral part of the culmen and in the pyramis. It is important to note that its fibers come mostly from the region of the trunk (463) because the nucleus dorsalis extends only from the last cervical or first thoracic to the first or second lumbar segments. The ventral spinocerebellar tract (of Gowers) arises in the posterior and intermediate horns of the gray matter of the same and opposite sides of the

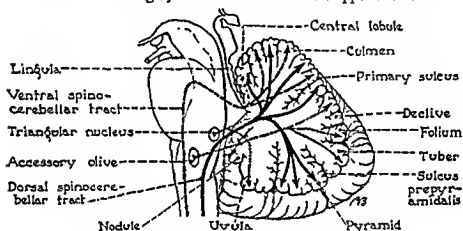


FIG. 100. Scheme of afferent pathways of the paleocerebellum and archicerebellum.

entire spinal cord. Its fibers pass to the ventral part of the lateral funiculus and then upward to the level of the fifth nerve where they turn abruptly backward to go via the brachium conjunctivum to the cortex of the lobulus centralis and culmen vermis, partly crossed. The vermis receives also afferent fibers from the opposite nuclei funiculi laterales (tractus tegmento-cerebellaris) and from the homolateral nucleus proprius corporis restiformis. There is also the important tractus olivocerebellaris from the opposite medioventral olivary nucleus. All of these follow the inferior peduncle into the cerebellum. The exact mode of termination of their fibers in the vermis is not known, although experiments on animals indicate a wide distribution.

The efferent fibers (Fig. 101) from the lobulus centralis, culmen, and

pyramis pass to the nucleus emboliformis, perhaps also to the nucleus globosus and dorsomedial part of the nucleus dentatus, whence new neurons go via the brachium conjunctivum to cross and end in the magnocellular part of the opposite red nucleus. The efferent fibers from the nucleus ruber magnocellularis cross almost immediately and descend in the spinal cord just medial and ventral to the crossed pyramidal tract (tractus rubrospinalis). The rubrospinal tract of man is very small when compared with the same tract in lower mammals.

The interrelations of the lobus mediodorsalis (declive, folium, ruber) are not so well known. This part of the vermis is related in some way to the hemispheres and does not properly belong to the spinal part (450). Similarly the lingula, uvula, and nodulus belong the vestibular part of the cerebellum as will be noted in the description of this part.

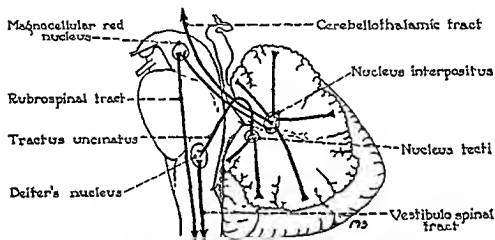


FIG. 101. Scheme of the efferent pathways of the paleocerebellum and archicerebellum.

The vestibular parts of the human cerebellum are much reduced in size. Judging from conditions in other mammals we may suppose that afferent fibers come from the triangular and ventral vestibular nuclei, perhaps also directly from the vestibular nerve, and pass via the inner part of the homolateral restiform body to the nuclei fastigii and to the cortex of the nodulus, uvula, flocculus, and lingula. The nucleus olivaris dorsalis also sends fibers to the opposite flocculus. The efferent fibers arise mainly in the nuclei recti (also probably some from n. globosus) and crossing curve anteriorly around the brachium conjunctivum to turn backward and downward into the opposite Deiter's nucleus and nucleus of the descending eighth tract. Because of its curved course this bundle is called the tractus uncinatus. Other fibers arise in the nuclei recti and

pass via the middle peduncle to the homolateral Deiter's nucleus (*Tr. fastigio-tegmentalis*). In mammals some fibers seem to go directly from the cortex of the anterior vermis to the ipsilateral Deiter's nucleus.

Any attempt to understand THE EFFECTS OF LOCALIZED LESIONS OF THE CEREBELLUM must take into account this fundamental subdivision of the organ into vestibular, spinal, and neocerebellar portions (286). To begin with the vestibular parts, they are so hidden beneath the main body in all mammals as to make an analysis of the effects of lesions in these regions very difficult. The vestibular nuclei lie in close proximity and are readily injured. The removal of the parts most readily accessible in the dog (nodulus and uvula) seems to cause the same symptoms as injury to the vertical semicircular canal of the labyrinth, namely turning over backward. Perhaps the distinction is of small importance for us. These parts of the cerebellum are much reduced in size in the human organ and lie so close to the vestibular nuclei that a tumor even of small size must involve both.

The effects of lesions of the spinal portions of the vermis may be analyzed best in birds where the hemispheres are absent (78). The bird, moreover, walks more or less erect on its hind legs as does man. It is known that if the cerebral hemispheres of a pigeon be removed by section anterior to the thalamus, the bird becomes somewhat somnolent and inactive but stands erect, walks and flies practically normally. The righting reflexes are, therefore, present and there must be a normal distribution of tone in the flexors and extensors of the lower extremities. If in such a bird the culmen (the only part of the vermis accessible and excitable) be stimulated electrically the animal sinks down on the side stimulated and only redresses his position when the stimulus ceases. The posterior limit of the region from which this effect can be obtained is marked by the sulcus primarius. If now a destructive lesion be made in the same region the pigeon assumes an attitude of opisthotonus with the neck curved backward and the legs rigidly extended. There is no nystagmus and no torsion of the neck and trunk. There is in other words an exaggeration of the normal standing position; the head is lifted too high and the extensors of the legs are contracted too strongly.

Somewhat similar effects may be obtained from the vermis of the cat (77) and in this animal the anatomical relationships of the effects are more evident because the vermis is more accessible. If in a cat in decerebrate rigidity the anterior lobe of the cerebellum be stimulated electrically, the extensor rigidity on the side stimulated disappears; it

may also be slightly diminished on the opposite side. A similar effect may be obtained by stimulation of the pyramis. Ablation of the anterior lobe (*culmen* and *centralis*) causes disturbances in the postural sphere: *increased tendon reflexes*, pronounced lengthening and shortening reflexes and gross exaggeration of positive supporting reactions (221). There is evidence even of localization within the anterior lobe (107).

These results of experimentation in animals indicate that the spinal parts of the cerebellum are concerned with modification of proprioceptive automatic standing. Is there any evidence that this is true in man? It must be admitted that the evidence is scanty (37). We may cite the case of the soldier who received a bullet in the vermis; the resulting symptoms affected almost exclusively the legs so that walking was practically impossible (315). Perhaps the most illuminating information has come from an analysis of the disease known as *primary paleocerebellar atrophy* (333). This strange malady develops often in the fifth decade of life. The patient complains always and principally of difficulty in walking. When examined one finds the outstanding difficulty to be of equilibrium. He can stand only by widening greatly his base and oscillates constantly forward and backward. Even when sitting some of the patients have difficulty in maintaining their equilibrium. When they try to walk they spread their legs widely apart and advance irregularly with many sudden deviations to the side and a tendency to fall backward. The *dysmetria* and *asynergia* of the lower extremities are less marked in other movements than walking. There is very little tremor. Both lower extremities are affected symmetrically. The upper extremities are much less affected and often nearly normal. Speech is hesitant and monotonous; *nystagmus* is practically absent. The lesion in the nervous system in such a case is found at necropsy to consist essentially of an atrophy affecting the cortex of the cerebellum, predominating in the superior vermis and the *antero-internal parts of the quadrilateral lobules*. The *dentate nuclei*, pontine nuclei and cerebellar peduncles seem intact. The postero-internal part of the olivary body may be degenerated. The degeneration is, therefore, predominantly in the spinal portion of the cerebellum.

This primary paleocerebellar atrophy seems to indicate that in man also the spinal portion of the cerebellar mechanism is concerned primarily with those muscles which maintain the erect posture and are used in progression, principally of the trunk and legs since the arms in man have been emancipated and are chiefly prehensile. There is, however, little to be seen of the series of symptoms so prominent in the lower mammals

which have to do with the stretch reflexes and supporting reactions. We may, therefore, safely predict that a tumor which develops in the vermis of the cerebellum will affect principally and symmetrically the lower extremities and cause a predominant difficulty in maintaining the erect posture and in walking. The exact relationship of these symptoms to the paleocerebellum and archicerebellum is still obscure; they resemble more the results of archicerebellar lesions in monkeys (221) which cause disturbances of gait and equilibrium without changes of tendon reflexes or postural resistance of the extremities. At any rate they arise from the vermis and not from the cerebellar hemispheres and are produced characteristically by the medulloblastoma which arises in the posterior part of the vermis. Thus is explained the frequent absence of nystagmus, the relative indemnity of the upper extremities, the symmetrical involvement of the lower extremities, with the gross difficulties of walking and maintaining equilibrium which are so characteristic of these children. They probably have an *archicerebellar syndrome*.

In the early stages of development DIAGNOSIS of these tumors must be made from all other causes of vomiting. Neatly every case is treated first as a gastro-intestinal disorder. The unsteady gait, the enlargement of the head and the squint, should, however, soon make the pediatrician shift his attention to the intracranial cavity. The disorder must later be differentiated from other causes of hydrocephalus. The ordinary so-called essential hydrocephalus begins in infancy. The only frequent causes of hydrocephalus, other than tumor, in children of ten years or more of age is intracranial extension of an infection of the middle ear or multiple tubercles. A history of infection of the middle ear may suffice to make the correct diagnosis in the former case although confusion may occur when both lesions exist simultaneously. The degenerative diseases causing disturbance of equilibrium, such as occurs in Friedreich's ataxia, make little difficulty because of the absence of vomiting, headache, enlargement of the head. There are also obscure intracranial affections in childhood which result in so-called chronic serous meningitis and which are differentiated with great difficulty from tumors in the cerebellar fossa (cf. p. 417); lately lead-poisoning has been shown to be the cause of many of these obscure cases (87).

But the medulloblastoma must be differentiated from other tumors in the posterior fossa in childhood. The graph reproduced in Figure 4, shows that the astrocytoma is even more common than the medulloblastoma. The differentiation is impossible to establish with certainty before

operation, although one may suspect an astrocytoma if symptoms have existed for a year or more, if the cerebellar disturbance predominates definitely on one side (because the astrocytoma more often occurs in the hemispheres) and if a *marked nystagmus* is present. At operation it is usually possible to distinguish between these two tumors. The astrocytoma is almost invariably subcortical, grayish and avascular, and almost always cystic. The medulloblastoma on the contrary is solid, reddish gray and vascular. The tumor which most closely simulates clinically the medulloblastoma is the ependymoma, which also often arises in the fourth ventricle of children. Vomiting is an early and prominent symptom in the clinical history of these cases also. At operation the ependymoma projects downward between the tonsils in the same manner. It is usually whiter, tougher, and its surface more irregular. The cerebellar hemispheres, moreover, separate readily from its upper surface because the tumor arises either from the floor of the fourth ventricle or from the velum medullare posterius. But it is usually necessary to proceed with a biopsy in order to be sure of the nature of the tumor during operation. The craniopharyngioma may rarely give rise to pronounced cerebellar symptoms. But it can cause confusion only in those cases in which suprasellar calcification is absent. The craniopharyngioma is a much rarer tumor and one does not make this diagnosis without serious reason. It is well to remember, however, that a tumor of the posterior fossa by producing a hydrocephalus of the infundibulum may cause many symptoms from the hypothalamic region.

The only logical TREATMENT for medulloblastoma cerebelli is complete removal, but this has so far proved impossible. However encapsulated the tumor may seem to be, and however complete the removal may seem to have been, the symptoms inexorably return in a few months. Even repeated radical extirpations have been of no avail. Unfortunately it is impossible to be sure of the diagnosis before operation. There is at least an even chance that the tumor may be an astrocytoma which can be removed and the patient permanently cured. At the present time, therefore, a suboccipital decompression is always made and the decision for further procedure must be made only after the dura mater is opened. Some surgeons still make an attempt to extirpate every tumor but until some new and more promising method of attack is devised it seems to me best to desist from such fruitless endeavor and be content with a decompression which usually suffices to relieve the block to the circulation of cerebrospinal fluid, or at best to remove only what comes

away readily without provoking too much bleeding.

It has been found that *the medulloblastoma is the most sensitive of all intracranial tumors to roentgen-radiation* (52) and for this reason it has been proposed to treat them by radiation before operation (146). If the patient improved promptly the diagnosis would be confirmed and the patient spared a futile operation. This proposal is logical; unfortunately radiation without previous decompression has long ago been proven dangerous, and the possibility of provoking the death, from bulbar compression, of a patient with a benign tumor has prevented this proposal from being generally adopted. Because of the tendency of the tumor to invade the leptomeninges, possibly aggravated by the operative interference, it seems best to radiate the entire central nervous system as soon after operation as possible. Even radiation, at first startlingly effective, causes but temporary improvement.

CHAPTER 12

ASTROCYTOMA

SYNDROME OF THE CEREBELLAR HEMISPHERE SYNDROME OF THE FRONTAL LOBE

During the discussion of the medulloblastoma in the cerebellum of children I remarked that nearly fifty percent of cerebellar gliomas were not of this malignant type but were on the contrary benign lesions with a good prognosis. These latter tumors are *astrocytomas*, the typical glioma durum of Golgi. Its prognosis is the most favorable of all the gliomas. When it occurs in the cerebellum it almost always causes symptoms in childhood.

This child (CASE XXV) of twelve years had such a tumor. She was always well until about three months before admission to the hospital when she began to vomit practically every day. Soon headaches began. She became weak and lost weight rapidly. About a month later she complained of pain and stiffness in the neck. Her mother noticed that the child did not use the right arm so well and staggered to the right when walking.

When admitted to the hospital she did not appear acutely ill but was rather listless and inactive. The suboccipital region was tender to pressure and the neck was held stiffly; any torsion or flexion caused headache. There was a horizontal nystagmus, with the quick component outward, provoked by looking to the extreme right or left, coarser and slower to the right. There was a slight weakness of the entire right facial nerve. The optic discs were choked about three or four diopters. Visual fields were normal. Roentgenogram of the head was normal. The extremities were hypotonic, especially the right. The right arm was very asynergic and fell away when outstretched, offering less resistance to displacement than the left. Her gait was unsteady on a broad base. She tended to fall to the right and deviated to the right in walking. There was slight hypermetria of the lower extremities, especially the right. There were no signs of pyramidal involvement and no sensory disturbances. The clinical impression was tumor of the right cerebellar hemisphere, probably astrocytoma.

A suboccipital exploration disclosed that the right cerebellar hemisphere was fuller and less vascular than the left. The midline of the

cerebellum was displaced to the left and the right tonsil was herniated into the foramen magnum. An incision into the cortex of the right hemisphere came down upon the surface of a grayish tumor at a depth of about one centimeter. The tumor was punctured and yellow clotting fluid obtained. The cystic cavity was then opened and about 30 ccm. of fluid removed. The cyst was completely surrounded by a shell of tumor about 3 mm. in thickness which was separated from the cerebellar tissue and removed. The resulting cavity was filled with normal saline solution, the dura mater was closed, and the wound sutured carefully. The patient recovered promptly. It is now two weeks after operation. The clicking of the optic discs has disappeared. There is no headache or vomiting. There is no nystagmus. The facial weakness has disappeared. You see that she walks quite steadily and when I ask her to touch my finger with her right hand there is no tremor or incoordination visible. The suboccipital region has a normal contour.

A comparison of the symptoms of this child with those of the little girl with the medulloblastoma (CASE XXIII) will reveal a marked contrast. Whereas the medulloblastoma caused disturbance of the lower extremities, and especially of walking, while the upper extremities were fairly normal and nystagmus was absent, in this little girl the disturbance predominated clearly in the right side, the arm was involved as well as the leg, and there was a marked nystagmus. The explanation of the difference in symptomatology lies in the fact that in this case the tumor was located in the right hemisphere of the cerebellum while the medulloblastoma involved mainly the vermis. In spite of the large size of the cystic tumor of this patient the symptoms of disturbance of the right cerebellar hemisphere were not very marked. The paucity of symptoms is due in these cases to the capacity of the nervous tissue to adjust itself and maintain its function when slowly distorted and compressed by a benign tumor. For this reason the symptoms of lesion of any part of the nervous system are much more strikingly apparent after sudden destruction by direct violence.

In the SYNDROME OF THE CEREBELLAR HEMISPHERE as produced by direct injury the symptoms are always homolateral, predominate in the extremities, and the arm is more affected than the leg whatever the region of the hemisphere involved. These symptoms may be detailed briefly as follows (262): The muscles feel flabby to palpation; the limbs are left in abnormal postures. If the forearm is held vertically the wrist on the affected side falls passively into extreme flexion. If the arm be

seized and shaken the hand flops about in an inert flail-like manner; the same may be done with the ankle. The lower extremity may be flexed until the knee touches the costal margin and the heel, the buttock. All of these phenomena depend upon relaxation of the musculature and are usually designated as indicating an *atonia*. There is also a moderate weakness of the involved limbs; they tire more quickly and the patient is reluctant to move them. The movements are, moreover, slower than normal; the initiation of movement is slower and relaxation also. These disturbances affect all muscles equally. The range of motion is not altered. There is, therefore, an *asthenia* of the affected musculature.

Most striking is the irregularity of movement. If a patient is asked to touch his nose with a finger of the affected arm, instead of the smooth, even, accurate movement of the normal limb, the movement is decomposed—the arm is first lifted from the bed and the elbow then flexed. Moreover, each movement is made in an exaggerated fashion so that the arm is lifted too high, the finger is brought too forcibly to the face and usually overshoots its mark. The same defects may be demonstrated in the lower limb by asking the patient to place the heel of the affected leg on the knee of the other. This decomposition of a complex movement into its elements is called *asynergia*. It results from the fact that the various muscles do not contract in proper sequence with the proper force while held in check by their antagonists. The overaction of the muscles is called *hypermetria*. The lack of the proper brakes on the motion can be demonstrated by asking the patient to flex his arm against his chest while the observer resists by holding the wrist. When the normal arm is released suddenly it is immediately checked, while the affected arm flies violently into the patient's face. The *asynergia* may also be demonstrated by asking the patient to make rapid alternate movements; the movements of the affected limb are slower and much less regular and uniform. This sign is called *adiadokokinesia*. When a purposeful movement nears or reaches its goal there often appear coarse irregular movements—a sort of tremor. The same tremor may appear whenever the muscles must maintain a posture, for example in the sitting posture there are often irregular oscillations of the head. All of the foregoing symptoms are often spoken of as *ataxia* or as *cerebellar incoördination*.

If the patient is now asked to hold his arms horizontally outstretched before him the affected one will slowly sag and deviate outward. If he is asked to lower the affected arm and return it to its former position, the arm returns outside and beyond; in other words the patient past-points to

the side of the lesion. The patient can stand alone either with eyes open or shut; there is no Romberg-sign. The head and trunk are inclined to the injured side; the homolateral shoulder is elevated. He can stand on the unaffected leg alone but not on the affected one. If pushed toward the affected side he staggers and is apt to fall. In walking, the asynergy of the affected leg is obvious in all its movements. The patient has a tendency to deviate abruptly or fall to the affected side. When the difficulty is slight it may be made more obvious by asking the patient to turn around quickly.

The eyes at first tend to be deviated slightly to the side opposite to the lesion. Any attempt to move the eyes from this neutral point results in *nystagmoid movements*, and the quick jerk is always lateralward and the slow movement toward the neutral point. The nystagmus is slower and coarser when the patient is looking toward the side of the lesion. There is a marked dysarthria. The speech is hesitating and slurred, and the force of phonation varies greatly. The ends of the sentences especially have a tendency to be explosive. Speech is accompanied by facial grimaces. The effect on speech seems to be the same whichever hemisphere is involved.

The tendon-reflexes on the affected side are often more difficult to elicit. A characteristic alteration of the knee-jerk can sometimes be elicited if the legs are allowed to swing freely. Whereas the normal jerk is brisk and quickly arrested, the affected limb moves leisurely and makes several pendulat swings to and fro before coming to rest. There is no alteration in sensation and no spasticity. The symptoms regress with the passage of time.

All of these symptoms may, from time to time, be produced by glioma of the cerebellar hemisphere (457), but vary in intensity in the different cases.

The uniform structure of the cerebellum suggests that it has a unitary function; but what might be that function, whose derangement could cause the symptoms just described, has never been determined to the satisfaction of everyone. A seductive hypothesis recently elaborated (180) holds that the cerebellum acts as a brake to prevent overaction due to inertia, the hemisphere exerting this influence predominantly on voluntary motion via the motor cortex (34). There is also no general consensus concerning the possibility of a localized effect being produced by a localized lesion of the cerebellar hemisphere. Certainly at the present time we do well in cases of cerebellar tumor to be able to distinguish

between the syndrome of the vermis and the syndrome of the hemisphere.

THE ANATOMICAL CONNECTIONS OF THE CEREBELLAR HEMI-SPHERES whereby these effects are produced are better understood (463). We have already remarked that the pontine nuclei and cerebellar hemispheres develop simultaneously with the cerebral cortex. It is not surprising, therefore, to find that there are robust tracts of nervous fibers descending from the cortex to the pontine nuclei. The frontopontine tract arises probably in the anterior central and posterior portions of the superior and middle frontal convolutions and descends medial to the corticospinal fibers in the cerebral peduncles. The temporopontine tract arises from posterior parts of the superior and middle temporal convolutions and descends in the cerebral peduncle lateral to the corticospinal tract; it is accompanied medially by the parietopontine tract. The corticopontine tracts all end in the homolateral pontine nuclei. The significance of the various cellular groups distinguishable in the pontine gray matter is not well understood so we need not enter into details concerning them. Suffice it to remark that in man the nucleus dorsalis is tremendously developed and that it is in this nucleus that the frontopontine tract ends. The dorsal nucleus lies in the rostral part of the pontine gray matter. The parietopontine fibers end most caudally, mainly in the nucleus peduncularis and medial part of the nucleus ventralis. The temporopontine tracts end in the intermediate regions, chiefly in the nucleus lateralis, nucleus dorsolateralis, and lateral parts of the nuclei ventralis or peduncularis.

The fibers which arise in the pontine nuclei (*tractus pontocerebellaris*) go almost exclusively to the opposite cerebellar hemisphere. It is possible that a few of them from the ventromedial part of the ventral nucleus end bilaterally in the vermis. They would transmit impulses from the phylogenetically older parietopontine radiation. But the relationships of the various nuclei to the cerebellar cortex are disputed. There seems to be general agreement only that from the ventral nucleus fibers go to the lobulus biventer. The arcuate nuclei are considered by some to be the most caudal pontine nuclei and fibers from them seem to go to the crossed anterior lobe of the cerebellum (*tractus arcuato-cerebellaris*); this tract is peculiar to man. Other afferent fibers to the cortex of the cerebellar hemispheres come from the opposite lateral nucleus of the inferior olivary body. This nucleus develops parallel with the cortex cerebri, the pontine nuclei and the cerebellar hemispheres. Its signifi-

cance is obscure but it seems to be an integral part of this complex mechanism. Fibers (tractus olivocerebellaris) leave the hilus of the olive, cross to the opposite restiform body (inferior cerebellar peduncle) and are distributed to the entire cortex of the heterolateral hemisphere. The details of their distribution are partially known (269) but not their significance.

The efferent fibers of the cortex of the hemispheres converge toward the dentate nucleus. From the latter the axones of new neurones pass via the brachium conjunctivum to the microcellular part of the opposite red nucleus. From there fibers pass upward to thalamus and cortex cerebri and an important bundle (tractus rubroreticularis cruciatus) crosses and descends toward the bulb.

If one adds to the above description the connections of the red nucleus and inferior olive with the striatum, thalamus and spinal cord an almost inextricable tangle results from which the final effector pathway to the extremities is not clear (Fig. 102); the rubrospinal tract prominently

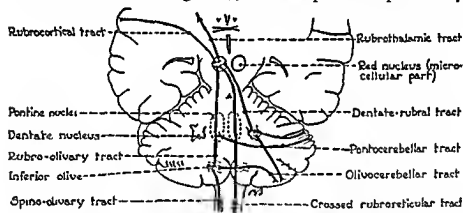


FIG. 102. Scheme of afferent and efferent pathways of the cerebellar hemisphere.

figured in textbooks is part of the efferent pathway of the vermis. The main efferent outflow from the cerebellar hemisphere seems to return to the motor cortex and reminds one strongly of the negative feedback mechanisms beloved of engineers.

When one remembers the extensive ramifications of this system of fibers one may understand that lesions anywhere from the frontal lobe to the spinal cord may give symptoms resembling those caused by lesions of the cerebellar hemispheres. In fact it is a tradition with neurologists that there is a special difficulty in distinguishing between tumors of the frontal lobe and of the cerebellum (243). We will turn, therefore, to the

former region for an example of the astrocytoma as it affects the adult patient.

This woman (CASE XXVI) of forty-five years has been somewhat depressed, inactive, and inattentive for two years. This state was in marked contrast to her former active cheerful self. She cried readily and took very little interest in her family. A sojourn in a sanatorium did not help her. She was not otherwise ill until nine months ago when she had a generalized convulsion, with loss of consciousness for half an hour. She felt tired for a short time afterward but remained well until a month later when her husband awakened one night to find her moaning and was unable to rouse her for a time. After a few weeks she began to have headaches, in the right frontal region at times but usually generalized. With these headaches she was apt to vomit. She complained of difficulty in seeing and glasses were fitted but helped her very little. In the last weeks she became much worse, had difficulty in speaking, spilled her food when eating, followed people with her eyes in a vacant stare and became drowsy and incontinent.

When admitted to the hospital she was dull, uncoöperative and did not answer questions. She yawned and rubbed her nose often. The nasal margins of the optic discs were hazy and the veins slightly full but no elevation was measurable. The visual fields could not be examined, because of lack of coöperation. There was a slight weakness of the lower left facial musculature on emotional stimulation only. The tendon-reflexes were brisk on both sides with a bilateral extensor plantar reflex. No sensory loss was demonstrated. The abdominal reflexes were not obtained. Strength was good in both hands but when an object was placed in the left one it closed firmly, was not relaxed on command and the object could only with difficulty be withdrawn from it. When placed on her feet she swayed and fell to the left if not supported.

The clinical impression was tumor of the right frontal lobe. A right osteoplastic exploration was made with local anesthesia. Before opening the dura mater, which was tense, an attempt was made to puncture the frontal horn of the lateral ventricle. At a depth of four centimeters yellow clotting fluid was obtained. The dura mater was then opened. An incision was made through the greatly flattened middle frontal gyrus which entered a large cavity at a depth of four centimeters. A large amount (50 or 60 ccm.) of cystic fluid was removed by suction. In the bottom of the cavity could be seen neoplastic tissue of which a fragment was removed for examination. Because of the unsatisfactory general con-

dition of the patient no attempt was made to remove the tumor. The patient did not immediately recover consciousness. The temperature rose rapidly to 40° and remained between 39° and 40° for three days. The bloodpressure rose to 156 mm. but the pulse rate remained between 130 and 140. There was a bilateral extensor plantar reflex. The pulse rate and temperature subsided suddenly on the fourth day and the patient awoke. It is now the fifth postoperative day and she has one symptom which we could not demonstrate before operation because of her semicomatose condition. Listen to this conversation:

"How are you this morning?"

"Fine, how are you?"

"Let me see you move your left arm. Try to move it."

"I have moved it." (No movement.)

"Let's shake hands," (holding out hand toward patient's left hand).

"You're a foxy one."

"Come on. Move your left arm."

"Wait 'til a more convenient time."

"It doesn't feel cold."

"How can it be when I am such a hot one everywhere else? Doctor, I want official permission to scratch."

"Where do you want to scratch?"

"Where it itches. The nurses keep me tired most of the time."

"How is that?"

"They bring me a long list of things to eat and I spend most of my day trying to decide what I want."

"Do you want to try to walk for us?"

"I'm a most unseaworthy craft and list to loo'rd."

You note the tendency to "wisecracking." This symptom, while it may rarely accompany tumors anywhere in the intracranial cavity, is particularly frequent with tumors in the frontal region. You will remark also that although it is impossible to get her to move the left arm spontaneously (she seems to be ignorant of its existence) the hand clasps firmly when I lay my finger within it. I have not been able to get her to cooperate for a sensory examination, but she winces when the arm is pricked with a pin. We will defer again the discussion of the nature of the tumor which was found in this patient and first consider the symptoms. Outstanding were the mental defects and the involuntary movements of the left hand.

There can be no question that MENTAL DISORDERS occur earlier and

are more intense when a tumor develops in the frontal lobe (48) than in any other part of the brain, except the corpus callosum and especially the region of the supramarginal gyrus of the left hemisphere. In the last situation there are special features of the mental defect which enable it to be recognized. These mental disturbances must be clearly distinguished from the global deterioration due to increased intracranial tension.

In fact it is a matter of universal experience that when a patient is afflicted with a high intracranial tension he becomes apathetic and torpid. He lies in bed with a dull and confused look on his face, putting his hand to his head in a dazed way at times, yawning and rubbing his nose. He pays little attention to his surroundings unless strongly stimulated. When questioned he responds slowly and with an effort as though it were difficult for him to collect his wits. All of his mental functions are slowed. His speech is correct but his memory is obviously deficient for recent events. Less often there is disorientation in time and place, illusion and fabulation. He is almost always conscious of his troubles and affected by them. Careful examination convinces one, however, that his intelligence is intact but merely veiled, as it were, or inhibited. This conviction is easily verified by giving the patient by mouth 45 ccm. of a saturated solution of magnesium sulphate. With the reduction of intracranial tension which ensues the normal mental alertness returns. This precaution should never be omitted when there is any doubt of the rôle of increased intracranial tension in the production of the mental disturbance. Because of the lack of control of this factor most of the published observations cannot be properly interpreted. One should not forget, however, that a long-continued intracranial hypertension due to internal hydrocephalus may cause a mental defect from actual destruction of cerebral tissue which will not disappear even though the tension be relieved. In any event late in the course of a tumor's evolution the mental poverty may be extreme so that the clinical picture resembles that of an advanced general paralysis or senile dementia.

The situation is quite different when the tumor arises primarily in the frontal lobe. The mental disturbance is then precocious and persistent even in the absence of intracranial hypertension. The first symptom is often forgetfulness. If the patient be a woman she forgets details of housework or to make the necessary purchases for the daily meals. If a man, it is remarked by his associates in business that he no longer retains the details of his transactions and later that he does not grasp readily new propositions. The patient may be conscious of these troubles and be

depressed by them but more often he is unconscious of them and more or less indifferent when they are pointed out to him. A young wife, for example, brought her husband complaining that whereas formerly he had been a loving and attentive husband, helping her with the housework and playing gayly with the children, lately he came home and sat in a corner doing nothing. If she remonstrated with him or asked him to do something he would comply but seemed no longer to have any interest in her or the children. Inquiry elicited no complaint from his employer but his work was of a routine manual character. His fellow-workmen remarked that he had become solitary and taciturn. He was found to have a meningeal tumor pressing on the anterior extremity of the left frontal lobe of the brain. At first such a patient's faults are mostly of omission but soon his mental deficit may translate itself into acts which show an evident lack of judgment. The business-man who has always been conservative and steady begins to make speculative ventures and ruins himself and his associates. One patient I remember who had been the best salesman in a large clothing-store. His employer was obliged to discharge him because when a customer was not pleased with the price he would reduce it to meet the customer's wishes. When his employer corrected him he defended himself with all sorts of bizarre arguments.

More frequent are lapses in the social realm. The patient ceases to observe those little social niceties which distinguish a person of good breeding. He may appear at social functions impropetly dressed and in general manifest an evident lack of interest in his personal appearance. His remarks are no longer quite proper, even positively indecent. Serious social aberrations may appear as in the case of the young wife who had always been a model of deportment, faithful to her husband, and careful of the children. Found in bed with a strange man one day when her husband returned from work she was ejected from her home and became an ordinary streetwalker. She was brought to the hospital later in an epileptic attack and found to be suffering from a tumor of the left frontal lobe of the brain. After its removal she returned to her husband and, although she continued to suffer from epileptic attacks, her conduct was thereafter quite correct. This young woman had one quite characteristic symptom. Ordinarily a patient in a hospital is fairly respectful and attentive to his physician, if for no other reason than that he knows he is more or less in his power. But this woman was wholly inattentive and uncoöperative and made the most scurrilous remarks concerning the physicians and nurses. This inattentive, uncoöperative, and disrespectful attitude is

not rare when a patient has a tumor of the frontal lobes.

It is often difficult to get these patients to take anything seriously. They often reply to all questions by making inane witticisms. The salesman just mentioned, when asked concerning his discharge, protested that he was the best salesman in the concern, that he could even sell a widow a suit of clothes with two trousers to bury her husband in. A better example of this silly jocularity was furnished by a formerly stolid workman who shocked his wife by holding the following conversation with me:

"How do you feel this morning?"

"With my fingers."

"I mean, do you feel well enough to go home?"

"Don't you think I belong better in the ashcan?"

"Will your wife not be glad to see you?"

"Oh, we have been married a long time; her ardor has cooled off."

"Why did you come to the hospital, anyway?"

"That's why. To get my battery charged."

Disorientation as to place may be quite pronounced. Many times I have remarked that these patients were unconscious of being in a hospital or, if aware of the nature of the place, thought it was located in another city. This symptom recalls the gross disorientation in space from which soldiers suffered who had been wounded in the frontal lobes; such a gross disorientation, however, I have never encountered from tumor in this region.

Generally these patients are indifferent, accepting such news as that they must undergo a serious operation with a shrug of the shoulders, but occasionally they may have sudden and inexplicable fits of anger and rarely spasmodic laughing or weeping. They are incapable of active attention and hence unable to work. Later the mental defect may progress almost to imbecility. The patient may become totally untidy, move his bowels, or pass his urine in bed and in general conduct himself in a totally demented fashion. He becomes incoherent, disoriented, and unconscious of his troubles. Such a mental disaster, before the occurrence of symptoms of another localization or in the absence of marked symptoms of intracranial hypertension, I have seen only with tumors of the frontal lobes, or of the corpus callosum in its anterior portion.

I have already mentioned the disturbances of psychic regulation which often accompany tumors in the region of the hypothalamus and will discuss later the profound and peculiar defects associated with tumors

centering around the left supramarginal gyrus. They are quite different from *the troubles I have just described which, when they occur early or in the absence of much intracranial hypertension, are quite characteristic of frontal tumors*. One meets occasionally the statement that the frontal lobes of the brain may be removed without any mental defect. This comes of confusing intellect with didactic knowledge. The most profound defects of the latter content of the mind result from injuries to the left occipitotemporal region. Injuries to the frontal lobes cause serious diminution of the ability to meet new situations and to orient oneself in society, more than an actual decrease in the amount of acquired information. It seems as though some control had been removed which enables one to guide himself in our complicated civilization so that the entire behavior of the patient is altered.

The other outstanding symptom which our patient shows is known as *forced grasping and groping* (1). It seems to be associated with lesions in the posterior upper and inner part of the frontal lobe, near the source of origin of the frontopontine tract, and can perhaps be produced also by lesions of this projection-pathway. Most commonly this symptom consists of a forcible grasping movement of the hand and fingers when an object is pressed into the hand. It is most readily elicited by stroking across the palm at the bases of the proximal digits. When the hand has closed firmly any attempt to remove the object only intensifies the grip. The patient is, moreover, unable voluntarily to relax the grasp. The phenomenon varies in intensity in different cases. It may be that the patient has never discovered it but some are certainly acutely conscious of it. One woman had learned to open doors with the left hand because she was unable to pass through once her right hand had grasped the doorknob. She had once smashed a dining-set when her hand clasped the table-cover as she passed by. If the patient makes no effort to open the clasped hand it is seen to vary in the intensity of its grip and finally relaxes. When the object is removed the hand may afterward make several incomplete grasping movements.

Many variations of this fundamental symptom occur. The touch of an object in the palm may be insufficient to provoke it and only a strong voluntary contraction will be followed by the persistent grip. A slow grasping movement may be made to light stroking of the fingertips, especially of the thumb and index. By repeating the stimulus the whole hand and arm may be made to follow as to a magnet. At other

times the patient may be able to deposit an object and relax his grip but before he can withdraw the hand it regrips the object. The phenomena of forced grasping and groping may occur in the absence of any demonstrable psychic disorder or weakness of the affected arm. Patients who are able to open and close the hand readily may be absolutely unable to relax this reflex grasp. But the symptom usually disappears as the voluntary paralysis becomes marked.

One of the most frequent signs of frontal tumor is facial weakness (418). It is contralateral and of typical central type, affecting only the lower part of the face. The frequency of facial palsy is doubtless due to the oblique direction of the anterior central gyrus which brings the area of the face much farther forward than the area for the arm or leg. The palsy is usually more evident on emotional than on voluntary stimulation. Often this weakness must be sought for carefully. There may be only a little flattening of one nasolabial fold or a slight lagging of one side of the mouth in talking. If one asks the patient to open the mouth as widely as possible the nonparetic side is lifted outward and upward more than the other and the platysma stands out on that side more prominently. The weakness may be brought out in other cases by asking the patient to make a violent physical effort such as to squeeze the hand tightly or to close the eyes firmly.

Of course, as the tumor increases in size the entire opposite half of the body is involved in the paresis with the production of typical spastic hemiplegia. In those cases of frontal tumor, as a matter of fact, which show well the symptoms of forced grasping and groping the leg is apt to be most affected in the contralateral hemiparesis; this is readily explained by the common location of the tumor, in these cases high up and posteriorly near the cortical leg-area of the anterior central gyrus. The involvement of the motor cortex may result also in convulsive attacks which may be focal or generalized. In the latter case the attacks are apt to begin with turning of the eyes and head to the opposite side. Convulsive seizures on the whole are not uncommon with tumors in the posterior parts of the frontal lobes and may begin very early. Temporary loss of speech may occur as a sort of aura before convulsive movements appear.

Nystagmoid movements of the eyes may occur, rarely as regular and sustained as those of a cerebellar nystagmus however. Anosmia is a rare symptom except in cases of meningioma of the olfactory groove. Rarely tremor of the hands or incoordination of gait may appear; they

are usually late symptoms. Another late symptom is anarthria if the tumor lies in the left hemisphere; it may be present only after convulsive attacks. There is also occasionally difficulty with conjugate deviation of the eyes to the opposite side.

I remarked before that the DIFFERENTIAL DIAGNOSIS between frontal and cerebellar tumor was reputed to be particularly difficult. I have not found it so. A good chronological history is often sufficient to distinguish them. It is true that late in the course of evolution of a frontal tumor, when intracranial tension is high, the patient may stagger when placed on his feet, as our patient did, and the head may be held stiffly. There also may be some irregular nystagmoid movements of the eyes and tremor of the hands. But characteristic cerebellar symptoms such as asynergia, dysmetria, dysarthria, hypotonia, and adiadokokinesia I have never observed (58). The mental obfuscation due to acute intracranial hypertension in cases of cerebellar tumor is usually easy to distinguish from the mental disturbances of frontal tumors, especially by examination after reduction of the intracranial tension by intravenous injection of hypertonic solutions. Moreover, if we but remember that cerebellar tumors are relatively rare in adults, and are on our guard, this error should rarely occur. In my experience the error made has almost invariably been to diagnose cerebellar tumor in the presence of frontal tumor and not the reverse; in nearly all these cases the supposed cerebellar symptoms were very dubious. One should have serious reasons for diagnosing cerebellar tumor in an adult; if the cerebellar symptoms are not definite one should seek confirmatory evidence from ventriculography.

The epileptic attacks may make one suspect a tumor of the central region but a tumor of the central zone never continues long to cause epileptic attacks without a paralysis ensuing; they are, moreover, usually accompanied soon by a loss of proprioceptive sensation. Whenever epileptic attacks recur over a considerable period of time without any paralysis other than a slight facial paresis the tumor should be suspected of being located in the prerolandic region. Tumors of the anterior extremity of the temporal lobe at times are difficult to distinguish. They cause mental disturbance, a facial weakness and, if on the left side, aphasia. Usually, however, the mental symptoms are slight and the aphasia more definite. Moreover defects in the visual fields, uncinate attacks, and other associated symptoms ordinarily aid the correct localization.

The greatest difficulty is to differentiate tumors of the frontal lobes

from tumors of the anterior part of the corpus callosum. The difficulty is sometimes insurmountable, the reason being that the corpus callosum is a great associating tract between the frontal lobes. The presence of bilateral pyramidal symptoms may make one suspect the correct diagnosis of callosal tumor in certain cases. The rather indefinite symptoms cult at times to determine which frontal lobe is involved. The facial of callosal tumors will be discussed later (page 298). It is often diffi-

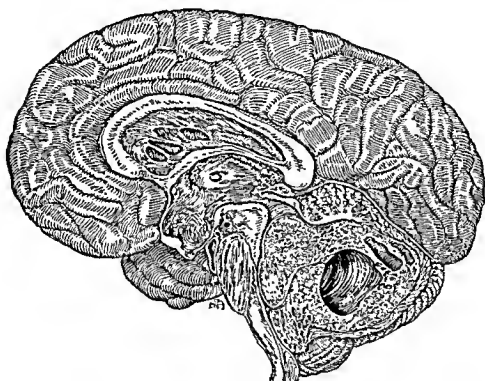


FIG. 103. Median section of brain with cystic astrocytoma of the cerebellum.

weakness I have found to be of the greatest help in this regard. The choking of the homolateral optic disc is said often to be greater, but I have found this too inconstant to be of value. Sometimes it is necessary to resort to a ventriculogram which for this purpose is very reliable.

The mental symptoms of tumor of the frontal lobes, before the onset of intracranial hypertension, may be confused with those of general paresis, senile dementia, or more often, presenile dementia. General paresis is usually excluded by the condition of the pupils and by the serological reactions, but presenile dementia is more difficult to differen-

riate and I have often been obliged to adopt an attitude of watchful waiting or to resort to ventriculography in order to establish the diagnosis. Twice I have diagnosed presenile dementia by biopsy of the cortex cerebri. We will discuss these difficult diagnoses in more detail later.

In both of the foregoing patients the tumor was of the same nature, a glioma of the type known as an **ASTROCYTOMA**. And it is a strange fact that these tumors usually cause symptoms during childhood when they are situated in the cerebellum whereas in the cerebral hemispheres they remain silent into adult life. The difference in part may be explained by the fact that cerebellar tumors in general cause symptoms earlier

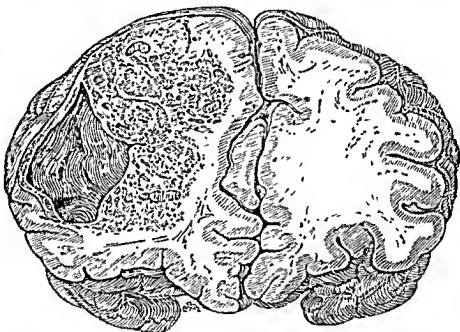


FIG. 104. Cross section of brain with cystic astrocytoma of the right frontal lobe, somewhat similar to the condition which must have existed in CASE XXVI.

because they are situated where they early block the circulation of cerebrospinal fluid.

It will be noted also that in both of our cases the tumor was cystic. The astrocytomas have a peculiar tendency to become cystic. The cyst has a smooth glistening lining and is filled with a straw-colored or sometimes orange-colored fluid which tends to clot when exposed to the air. The fluid's content of albumen is very high and its color is due to the presence of bile-pigment. The cyst seems to be formed by a

liquefaction of the neoplastic tissue but the cystic fluid is undoubtedly formed mainly by transudation from the bloodstream. If emptied out the fluid is rapidly reformed and is soon under a high tension. At some part of the wall of the cyst is usually to be found a mural nodule, or larger mass, of tumor. It projects into the cavity irregularly; often it has a yellowish or grayish color. At times the cyst is completely surrounded by tumor (Fig. 103), or one part of the wall is tumor which does not project into the cavity (Fig. 104).

But astrocytomas may be solid. Such tumors, and the mural nodules of the cysts as well, are usually *firm* and *avascular*. The cut surface is grayish in color, approaching that of the cerebral gray substance.

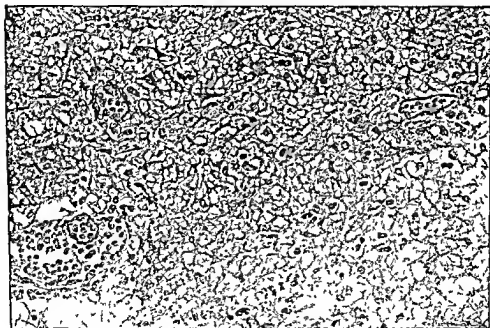


FIG.105. Drawing of microscopical preparation of an astrocytoma

Small cystic cavities are usually scattered throughout but rarely hemorrhages or fatty degeneration. These tumors were called by the older pathologists *glioma durum*. These tumors are not clearly circumscribed although they may seem to be when examined with the naked eye. It is possible at operation to think one has found a capsule because the cerebral tissue is so much softer that a false line of cleavage may easily be forced in an attempt to enucleate the growth. Some astrocytomas, however, particularly of the cerebral hemispheres, are soft and mushy in consistency.

The MICROSCOPICAL STRUCTURE is quite typical (Fig. 105). The astrocyte was for long the only interstitial cell which could be clearly identified, particularly after Weigert had perfected his method for the fibrils of the fibrillary ones. For many years, therefore, these fibrils were searched for in brain-tumors and when found a diagnosis of glioma was made. The demonstration by Cajal of the protoplasmic astrocytes of the cerebral cortex soon led to the recognition of the other astrocytomas in which the cells did not form fibrils. We recognize, then, astrocytomas of protoplasmic and of fibrillary types but most of them are transitional (88). A typical fibrillary astrocytoma when examined at low magnification is seen to be composed essentially of a feltwork of fibrillary material within which are scattered nuclei and small bloodvessels. The feltwork can be shown to consist not alone of fibrils but also of numerous protoplasmic processes of the astrocytes. At a high magnification the star-shape of the neoplastic cells is evident; nearly always the cells have many processes which leave the perinuclear cytoplasm in all directions. Within the processes lie the fibrils. The perinuclear cytoplasm is usually very scanty but a characteristic early degenerative change results in a swelling and hyalinization of the cell-body and the displacement of the nucleus to one margin. The nuclei are oval with a fine network of chromatin. The nucleoli are not prominent. Mitotic figures are rarely seen. Bloodvessels are scarce and have thin walls of connective tissue. The neoplastic astrocytes rarely have well-developed vascular processes, but the processes seem to form a sort of glial wall around the vessels. Here and there the tissue seems to undergo a liquefactive necrosis which results in the formation of cysts filled with a homogeneous jelly-like substance; in these regions the meshes of the feltwork may be much distended. In other areas the fibrils are compressed into parallel bands by the pressure of the cystic fluid. Hemorrhages and fatty degeneration are rare. Not all of the cells have the typical star-shape. Many are fusiform with, however, several fibrillary processes extending from the poles. These fusiform cells may have considerable cytoplasm containing granules of unknown nature, rarely pigment. Typical astroblasts are uncommon.

The relative number of fibrillary and protoplasmic astrocytes varies in different astrocytomas. Those of the cerebral hemispheres of adults are often composed of protoplasmic cells; these are soft, friable growths. They are peculiarly liable to a sort of hyaline transformation of the cells with matting together of the processes so that a pseudosyn-

cytium results. The protoplasmic tumors give much more evidence of growth. Multinucleated cells are frequent and appearances of amitotic division of the nuclei are found. In some areas collections of spongioblasts may give evidence of the possibility of malignant "dedifferentiation." The protoplasmic astrocytomas also are usually cystic. The cysts have a characteristic smooth shiny lining which is composed of compact processes and fibrils of the neoplastic cells.

There is at present no means of making a DIAGNOSIS of astrocytoma before operation. At operation the grayish avascular neoplastic tissue is fairly characteristic, but a spongioblastoma or ependymoma may look very similar. The finding in the cystic cavity of clear, yellow fluid which clots when exposed to the air is presumptive evidence only, because such cysts are found also in other gliomas. However, in the other frequent type of glioma—glioblastoma multiforme—the fluid is darker due to the presence of hemosiderin and cloudy from debris and fat. The cyst of an astrocytoma is smooth-walled and glistening; that of the glioblastoma multiforme is a ragged cavity rather than a cyst. It is sometimes difficult to distinguish microscopically the astrocytoma from a gliosis. The distinction may usually be established from an examination of the vascular processes, which are prominent in a gliosis and feeble in the astrocytoma. The gross appearance may help, since the astrocytoma is an expanding lesion and the gliosis a contracting one.

The TREATMENT of astrocytomas is very satisfactory. They are essentially benign lesions, although there is evidence that the protoplasmic ones may rarely undergo a malignant "dedifferentiation" especially in the cerebral hemispheres. Moreover, they are relatively avascular which makes their surgical manipulation easier. The fact that they are often largely cystic reduces the mass of the tumor and the emptying of the cyst gives the surgeon room to manipulate. Provided the mass of the tumor does not lie in a vital spot of the brain these tumors may be extirpated with confident expectation of permanent relief. It should not be forgotten, however, that when a cyst is present it is necessary to remove the mural tumor else the cyst will refill and the symptoms will soon return.

CHAPTER 13

OLIGODENDROGLIOMA

SYNDROME OF THE PARIETAL LOBE THALAMIC SYNDROME
SYNDROME OF THE APHASIC ZONE

Since the oligodendroglia is so closely related to the neuroglia and all transitions can be found normally between the two types of interstitial cells one might confidently expect to find also gliomas composed essentially of oligodendroglia. I first published (51) this hypothesis in 1924, but only recently have the methods of demonstrating oligodendroglia become sufficiently perfected to establish this type of glioma as a definite entity (44).

Oligodendrogliomas are predominantly tumors of the cerebral hemispheres of adults but are not the only gliomas which occur there. Three types of glioma are frequently found in the cerebral cortex—the protoplasmic astrocytoma, the oligodendrogloma and the glioblastoma multiforme—but none of them has any definite predilection for a particular region of the cortex. It so happens that our cases of oligodendrogloma have marked sensory symptoms so that it will be convenient to discuss the sensory system in connection with them.

The first patient with a tumor of this kind which I wish to demonstrate was operated upon only three days ago and is still rather ill but I have chosen her because of interesting sensory symptoms which I fear will disappear in a few days. She is a housewife of forty-one years (CASE XXVII), previously well except for a transitory jaundice, "nervousness," and occasional headache. Just six months ago she began to suffer from almost constant diffuse headache. Three months later double vision occurred so that since that time she acquired the habit of keeping the right eye closed. Occasionally she vomited but complained of no other symptoms except photophobia for the last few weeks.

When admitted to the hospital she was disoriented, restless and inattentive. There was a weakness of the right external rectus muscle, a few unsustained nystagmoid movements on lateral deviation of the eyes, and bilateral choked discs of four diopters elevation. The other cranial nerves were normal; there were no signs of lesion of the pyramidal tracts and no sensory changes could be determined. There was

a right upper homonymous defect in the visual fields (Fig. 106). General examination of the viscera was normal. In the roentgenogram was seen a diffuse calcification of the left occipitotemporal region (Fig. 107). From its situation and character the calcification was judged to lie within a glioma. Because of its situation also, presumably underlying the posterior temporal and angular gyri, it was thought probable that unless the tumor happened to be cystic little could be accomplished except to remove the bone and leave a decompression.

An osteoplastic exploration was made in the left occipitoparietal

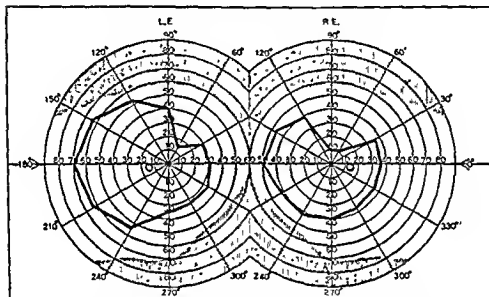


Fig. 106. Visual fields from CASE XXVII before operation.

region with its base in the temporal region. The dura mater was very tense. An exploring needle entered a cystic cavity at a depth of four centimeters and a little yellowish fluid spurted out under great tension. This was immediately followed by bright red blood. The dura mater was then opened hastily. The brain herniated slowly and progressively through the opening. It was thought that a hematoma was forming in the depths; so an incision was made into the cortex high up, as near the midline as the bony opening permitted, and was rapidly carried downward and inward until tumor was encountered. A large portion was removed with an electric scalpel. No hematoma was encountered. At the end of the procedure the tension of the brain had been relieved, but the cortex which had been undermined looked to be badly contused.

The patient recovered promptly from the operation although collections of cloudy fluid, resulting from the use of the electric scalpel, have had to be repeatedly evacuated from under the bone-flap. She is oriented and surprised to find herself in Chicago. She feels quite well except that she has difficulty in speaking. Analysis of the difficulty of speech indicates that comprehension of spoken language is little if at all affected, but reading is impossible. There is some difficulty also in finding words and in naming objects, but expression of speech is intact. We will return to these troubles later.



FIG. 107. Scheme of roentgenogram from CASE XXVII. Calcification in left occipitotemporal region. Compare Plate VI.

She complains principally of difficulty in using the right arm. When we examine it we find it quite flaccid but the strength of the various muscles is practically as good as that of the corresponding muscles of the left arm. The tendon-reflexes are equal in the two arms. Nevertheless it is very difficult for the patient to perform purposeful movements with the right arm. If I ask her to drink from this glass of water, the movement of the hand toward the mouth is irregular, the mouth is missed and the water spilled. The difficulty of using the

arm is much greater when the eyes are closed. The patient herself is quite conscious of this fact and complains that when the right arm is under the covers of her bed she loses it and does not know where it is until she can see it again. If we now extend the two arms symmetrically on the bed and close the patient's eyes, after a few moments you see a strange phenomenon. The right arm begins to make irregular movements and soon wanders to a considerable distance from its original place. The patient meanwhile is quite unconscious that this arm has changed its position; the sense of position in this arm is totally lost. She does not know when I manipulate the fingers whether they are flexed

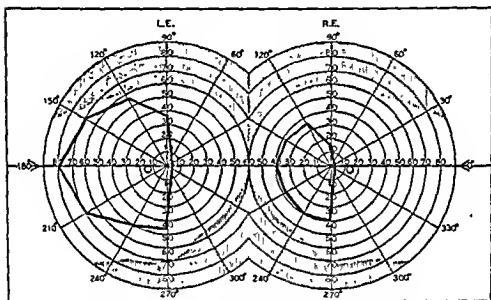


FIG. 108. Visual fields from CASE XXVII after operation.

or extended. Furthermore she is incapable of recognizing objects placed in her right hand. You may think this is due to her inability to manipulate the objects, but in the left hand she recognizes the same objects promptly when they are merely pressed against the palm although occasionally she is at a loss for the name of the object and has to indicate its use by gestures. The sensory loss in the right arm has been very carefully analyzed. There is a complete astereognosis and complete loss of sense of position. Touch is less acute over the right arm than over the left and she is unable to locate a touch or to discriminate two points. Pain and temperature are felt all over the right arm but less acutely than over the left one. Vibratory sensibility she insists is more

acutely felt over the right arm. No sensory or motor disturbance can be found over the leg and trunk. There is also a complete right hemianopia, except for the macula (Fig. 108).

Aside from the nature of the sensory loss, the limitation of the defect to the arm is sufficient evidence that the causative lesion is cortical, an acute cortical damage at the time of operation. And you should note that there is not a general decrease in sensory acuity over the arm but that the sensory loss affects variously different senses; in particular pain and temperature are little affected. We are apt to think that all

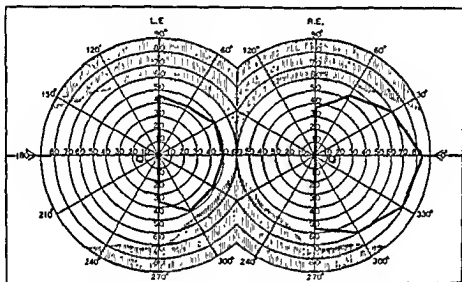


FIG. 109. Visual fields from CASE XXVIII.

conscious activities reside in the cortex but there is much evidence to lead us to believe that the thalamus is able, in the absence of the cortex, to perceive painful stimuli. At any rate it is certain that lesions of the thalamus cause not only alterations of sensibility but actually spontaneous pains in the opposite half of the body. These alterations of sensibility are so characteristic that they are spoken of as constituting part of the thalamic syndrome.

I have never observed a fully developed thalamic syndrome in a case of tumor of the brain but this second patient has undoubtedly evidence of involvement of the thalamus. He (CASE XXVIII) is a man thirty-seven years of age who was always well until a year ago when he began to suffer from double vision. Two months later the right eye-

lid began to droop and after a few weeks he could no longer raise it. About this time he began to be drowsy and had great difficulty in staying awake at his work. He had no pain or discomfort and came to the clinic five months after the onset because of the trouble with his eye.

There was found to be a complete paralysis of the third and fourth cranial nerves of the right side. The visual acuity of the right eye was

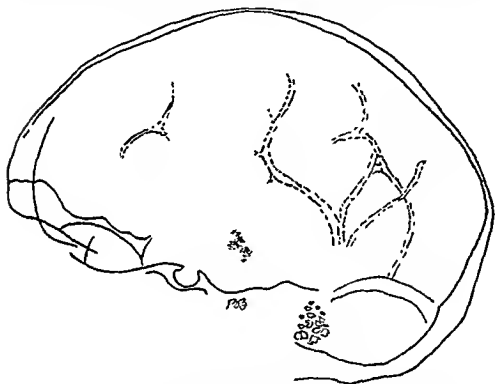


FIG. 110. Scheme of roentgenogram from CASE XXVIII. Calcification behind and to the right of the sella turcica.

0.3+1 and of the left eye 1.0+2. There was a left homonymous hemianopia involving also the macula (Fig. 109). The fundi appeared normal; there was no choking or atrophy of the optic nerves visible. No other paralyses or loss of sensation could be found but roentgenogram of the head revealed a patchy faint area of calcification about 8 mm. in diameter lateral to and slightly behind the sella turcica in the right temporal fossa (Fig. 110). The sella turcica itself was normal and so were the optic foramina. The patient was alert and coöperative. A diagnosis was made of calcified tumor of the inner part of the right temporal lobe. A decompression was advised as a preliminary to roentgen-radia-

tion since little hope was entertained of accomplishing the removal of the growth unless it were cystic.

An osteoplastic craniotomy was therefore made in the right temporal region and an immediate subtemporal decompression performed. The dura mater was not tense. It was opened in the temporal region. The exposed surface of the temporal lobe appeared practically normal. An incision through the second temporal convolution entered the temporal horn of the lateral ventricle. Another incision was made lower and anteriorly; at a depth of 5 cm. it came upon the surface of a tough grayish mass, not clearly separable from the cerebral tissue. Fragments were removed for microscopical study which proved the tumor to be an oligodendroglioma. After operation the patient was very drowsy and his left arm was weak. He had also a low fever and bronchitis for several days. He gradually improved and was discharged three weeks after the operation. At that time he was still drowsy. The palsy of the third and fourth nerves was still complete and the hemianopia persisted as before. The decompressed area was not bulging.

It is now four months after operation. He has been given extensive roentgen-radiation. He has deteriorated mentally as is quite evident from the fact that his bed is smeared with feces. He is obstinate and uncoöperative. The decompressed area is soft and bulges only slightly. There is still a complete palsy of the third and fourth nerves of the right side, and a left homonymous hemianopia. There is evident primary atrophy of the right optic nerve; the left is practically normal. There is a slight left facial weakness evident on emotional stimulation. The tendon-reflexes on the left side are brisker and there is an extensor plantar reflex. There is a left hemiparesis but without clonus or spasticity.

His wife, who is a trained nurse, tells us that he does not like to have the left side of his body washed and yesterday he would not allow the barber to shave the left side of his face. In spite of his uncoöperativeness we can perhaps determine the nature of this hypersensitivity. He does not respond to touch on either side of the body but this is due simply to obstinacy or drowsiness or both. To pinprick on the right side he responds by withdrawing the limb pricked or by rubbing the pricked part, locating the stimulus fairly accurately. On the left side he complains bitterly of a pin-prick but makes no attempt to brush away the offending stimulus. To a tube of hot water he makes no response and very little to cold water on the right side but makes bitter complaint if touched with a cold object anywhere on the left side.

It is impossible to make a complete and careful sensory examination but we have enough evidence to conclude that the neoplasm has invaded the optic thalamus.

You may recall that the thalamus is composed of a dorsal part, the thalamus proper, and a ventral part called the subthalamus. The latter is an important motor coördinating center and receives fibers from the dorsal part of the thalamus and from the corpus striatum. Its principal nucleus is called the nucleus subthalamicus (of Luys). Lesions of this body cause *irregular movements*, of the opposite extremities, known as *hemiballismus* (335). The thalamus proper (488, 105) contains many nuclei which may be divided into a phylogenetically older group, situated medially and consisting of the medial and anterior nuclei, and a neothalamus which is an appendage of the cerebral cortex. The neothalamus contains the nuclei ventrales lateralis et posterior (which receive the medial, spinal and trigeminal lemnisci), the pulvi-

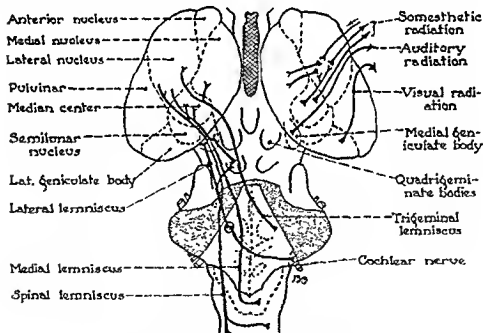


FIG. 111. Scheme of the thalamus and its connections (after Herrick).

nar, the lateral geniculate bodies (which receive the optic tracts), and the medial geniculate bodies which receive the acoustic lemniscus (Fig. 111). Injury to the nuclei of the neothalamus will therefore cause varied defects of sensation depending upon the exact nuclei involved, but

when one speaks of the THALAMIC SYNDROME ordinarily a very definite association of phenomena in one half of the body is meant (251), to wit:

1. A hemihypesthesia involving more the deep sensibility than the superficial.
2. Hemiastereognosis, more or less complete.
3. Persistent, paroxysmal, intolerable, spontaneous pains in the side involved.
4. Sometimes choreoathetotic movements, hemiataxia, or even a mild, usually transitory, hemiparesis. These motor symptoms result largely from involvement of adjacent structures, notably the subthalamus, and are often absent.

The most characteristic examples of this thalamic syndrome are produced by thromboses of the posterior cerebral artery (198), and the lesion usually involves the posterolateral part of the lateral nuclear mass. The alteration of sensibility in these cases is quite unique. The spontaneous pains may occur in any part of the half of the body involved. They are not sharp definite pains but are described as boring or tearing; at any rate they are so disagreeable to the unfortunate patient that they may even drive him to suicide. Paresthesias of other types may also be present in the nature of tickling, crawling sensations. All these disagreeable impressions are exaggerated by cold and calmed by heat. Any emotion is also apt to increase them, especially sadness. When examined objectively one finds tactile, painful, and thermal sense of diminished acuity but the defect involves especially the deep sensibility so that sense of position and stereognosis may be completely lost. Although there is a hypo-algesia, painful stimuli nevertheless have a very disagreeable quality and radiate from the area stimulated. Aside from the spontaneous pains with their characteristic exacerbation by cold and emotion the sensory loss resembles that due to lesions of the cerebral cortex and this is readily understandable when we remember that the neothalamus is the last relay-station in the pathway of sensation to the cortex.

The SENSORY LOSS FROM LESIONS OF THE CEREBRAL CORTEX (251) is always confined to the opposite half of the body and predominates in the limbs, particularly their distal parts. All forms of sensation are disturbed by lesions of the cortex, but very unequally. Sensation of pain is least altered, at most the patient may state that pin-prick is plainer on the unaffected side of the body. The distinction of minor

differences of temperatures is more difficult after cortical lesions but rarely is there any marked loss of thermal sensibility. There is usually little alteration of tactile sensibility by the usual examination with cotton-wool, but more careful examination will demonstrate a great irregularity in the patient's responses and a threshold for tactile sensation cannot be obtained. Sensibility to vibration is unaffected.

More distinct losses in sensitivity occur in the field of the proprioceptive senses. A patient after a cortical injury is no longer able to appreciate the extent or direction of movement of the joints, or the position of parts in space, and so also unable to appreciate differences in weight. The ability to recognize the shape of an object placed in the hand is often lost; this ability is known as stereognosis and should be clearly distinguished from the capacity to identify objects under the same conditions. The latter capacity is also disturbed by lesions of a nearby part of the cortex. Stereognosis is usually lost along with loss of sense of position and inability to localize touch.

It is known that the location of a tactile stimulus is very accurately appreciated over the extremities and face, although less certain over the trunk, particularly the back. After lesions of the sensory cortex this capacity is grossly disturbed. The discrimination of the quality of tactile stimuli is also disturbed; it may be tested in many ways but in the clinic it is usually done with a compass. The distance of separation of the two points necessary for them to be perceived as two stimuli when simultaneously applied to the skin is taken as a measure of the delicacy of tactile discrimination. The disturbances of general sensibility from cortical lesion most easily demonstrated are difficulty of recognition of posture, distinction of form and two-point discrimination.

The zone of the cerebral cortex from which these disturbances may be obtained includes the posterior central gyrus, the superior parietal lobe, and the supramarginal gyrus, at least in part. There is no general agreement as to the distribution of the different modalities of sensation, but it seems that the more complex disturbances, such as *astereognosis*, may be elicited from a much larger area than the simpler disturbances, such as loss of sense of position which is much more profound as the posterior central gyrus is approached. Much more certain is the regional distribution of the sensory changes. There is no doubt that the distribution in the posterior central gyrus corresponds to the motor distribution in the anterior central gyrus, the leg being represented nearest

the midline, followed by the trunk, arm, and face. The ulnar border of the arm is nearer the midline than the radial. Numerous cases of cortical aesthesia have been observed in which the radial border of the hand was involved simultaneously with the face, especially the corner of the mouth. The neck seems to be near the trunk. The representation of the limbs is much more extensive than that of the trunk and the area of the hand and fingers is particularly extensive. Anesthesias confined largely to one or two fingers have been observed.

Each of these two patients has a hemianopia, but the visual pathways are injured at a different level in the two cases. The first patient had an upper quadrantic defect before operation, clearly caused by lesion of the optic radiation. This defect was completed to a hemianopia by operative trauma of the parietal region. An isolated lesion of the parietal lobe will sometimes cause a lower quadrantic defect although this is much less frequent than the upper quadrantic defect of temporal origin (cf. p. 289). The second patient had a complete hemianopia at the onset even before any symptoms of increased intracranial pressure appeared. The associated lesion of the third and fourth nerves makes it probable that his hemianopia was the result of involvement of the optic tract (319).

We noted that the first patient had difficulty in reading and in naming objects. She read too rapidly for us to examine these defects in detail. It is, however, very important for the physician to be able to recognize difficulties in speech of cerebral origin and to be able to evaluate them correctly because the cortical mechanism of speech is located in the left cerebral hemisphere of right-handed persons and the character of the defect in speech varies with the location of the lesion in this hemisphere. To give you some idea of the nature of these cerebral defects of speech, or APHASIAS as they are called, I have brought up this other patient (CASE XXIX) who has a global defect involving almost all aspects of speech. He is a well-educated man of fifty-seven, a teacher of manual training in a high-school. He had always been well and efficient in his teaching until some three months ago when he began to have difficulty in finding words to express his thoughts. We need not go into details concerning his history which is irrelevant here. Suffice it to say that he was operated on some weeks ago and a cortical glioma was removed from the region of the supramarginal gyrus of the left hemisphere. He did not have before operation, nor has he now,

any signs of increased intracranial tension. All of his symptoms are due to destruction of cerebral tissue by the tumor. He has now returned to the hospital for further roentgen-radiation. You saw that he walked normally into the room, took a chair, picked up the newspaper and looked at it listlessly, put it down again and now sits with a dejected look on his face. There is no defect in his visual acuity; he sees quite well what is in the paper. If we try now to engage him in an ordinary conversation you will soon perceive his real difficulty:

"How have you been feeling these days?"

"Slipping around— broken— Let's see—."

"How have you been feeling these days?"

"When you came out you felt pretty good— and I don't know any more."

"What do you do at home these days?"

"I don't do anything, doc" (laughs).

"Have you tried to do any manual training work?"

"Not since you've been here. I don't get a chance."

"Do you have any children?"

"Nobody but two boys— the old boy is president— no— he works— anyhow he works in the city— and the older one works at school and is at home."

"How old are they?"

"Oh! the old one is twelve— no, the oldest one is fifteen— and the other one is twenty— no fifteen or something like that— fifty-five or six— no, he takes less than that."

"Where were you teaching school?"

"I was— isn't it funny to take a dig down like that— oh, I just don't know anything" (weeps).

You have seen that he is rarely able to say what he wishes to say, is conscious of his defect, and deeply affected by it. In the course of the conversation other typical aphasic alterations of speech occurred. He spoke of himself in the second person; this is called *agrammatism*. He misused words; this is called *paraphasia*. And he repeatedly used the same word where it was not appropriate; this is called *perseveration*. We will now try to analyze his difficulty in more detail and begin by testing his comprehension of speech. In making this examination one should always begin with simple tests.

"Close your eyes." He does it promptly.

"Put out your tongue." This is also done correctly.

"Put your finger on your nose." You see that he first put out his tongue again, seemed puzzled and now looks inquiringly at me.

"Put your finger on your nose." He stops to think, tries to repeat the command and is completely lost.

"Take off your glasses." He does so immediately.

"Put your finger on your nose." He hesitates and then places his finger on his cheek.

"Show me your nose." He is unable to do so and says, "You get me mixed up."

"Show me your ear." He does so correctly.

"Put your finger on your ear." It is promptly done.

"Put your finger on your nose." He does so at once, an instance of the typical variability of response so characteristic of cortical lesions as we saw also in studying the sensory defects of the former patient.

We have easily demonstrated that this patient has a relative incomprehension of oral language. With patients having slighter aphasic defects it is necessary to use more complicated demands and in particular those involving the distinction of right and left. Another favorite test I am sure this patient will be incapable of executing. I place before him three blocks of varying size and command him to keep the large one for himself, to throw the small one on the floor and to give the middle-sized one to me. He hesitates and finally executes at random. Responses involving movements of the extremities as evidence of comprehension are used because there is often a concomitant disturbance of verbal expression whereas the use of the hands is less often disturbed. Writing is sometimes used as a medium of expression by these patients, but is also frequently disturbed.

We saw him looking at the newspaper a while ago. Let us see whether he can read. He takes the newspaper and turns it around. I gave it to him intentionally upsidedown. He begins to spell, pointing to the letters with his finger. (BONUS) "I can't tell— O— Man— I can't get it— G"; (GIVEN) "G-I-N-E-N"; (BECOMES) "B-E-G-O-M-E-G"; (MONTHS) "M-O-M— can't get it— H— G." He skips many words and makes no attempt to pronounce the words he has spelled. It is obviously too difficult for him. I will print simpler words for him and show them to him so that he gets a total impression of a single word. (NOSE) correctly read. (EYE) correctly and promptly read. (EAR) "E-E- That's just an E." (EYE) "E-E-." (NOSE) correctly read. (HAND) "E-E-." (NOSE) "nose." (HAT)—"hat." (EYE) "eye." (DOG) "dog."

(CAT) "cat." (EAR) "E—east"—lost— (NOSE)— "gave it the wrong dog"— (HAND) "hand." You doubtless have remarked again the variability of response and the perseveration. We will try him with simple written commands. (CLOSE YOUR EYES). He reads it aloud correctly to our surprise but makes no attempt to carry out the command. When told to read it and do what it says he reads again correctly but makes no attempt to execute the order. It is obvious that he has great difficulty in understanding written language. This difficulty is known as *alexia* but varies in different patients from an inability to grasp completely the meaning of a paragraph to an inability to interpret even single letters.

I have asked to have his lunch served to him here. I want you to observe that he eats without any difficulty. He has apparently no trouble with manipulating common objects. Yet yesterday he was taken to the department of occupational therapy, given materials and tools and told to build a bird-house. He began at once, was disgusted with the saw, sought about for a file but was unable to use it in sharpening, then proceeded to measure out and construct the house which you see here. It would be a creditable performance for a beginning student but not for an instructor. It is very evident that the edges are not even and the angles not square. There is difficulty especially if he is given a strange task to perform. He has told me that he never smoked. We will give him a cigarette and a box of matches, a common test for these troubles, and see what he will do. He puts the cigarette in his mouth, opens the box, takes out a match, scratches it, and lights the cigarette. Then he holds the match without extinguishing it until it burns his fingers. He tries to blow it out without taking the cigarette from his mouth, shakes his hand because of the pain and makes a whistling noise with his mouth which allows the cigarette to fall. He looks rather sheepish. The difficulty in manipulating objects in the absence of paralysis or sensory disturbance is called *apraxia*. It may be almost purely a difficulty in initiating voluntarily movements of the arm; it is then usually unilateral, involves the left arm and is often accompanied by some paresis of the right arm. When it involves the right arm this motor apraxia is usually complicated and masked by the paresis of the same arm. When the apraxia is bilateral it is never purely motor but is accompanied by aphasic, sometimes by sensory symptoms, and is called ideomotor apraxia to indicate that it is secondary to a more fundamental mental deficit. Of course a patient may be unable to perform certain acts purely from an intellectual deficit; he is then said to have

an ideational apraxia, but the term apraxia really should not be used for the troubles of manipulation observed in profound dementia or amentia.

Much more striking is the fact that the patient has lost not so much the use of objects but their names. This can be easily demonstrated.

"What do you have in your hand?" (toast)

"I've got—this—bread."

"What kind of meat is on your tray?" (bacon)

"This is—was—I don't know."

"What is in your cup?" (coffee)

"It's a—ob, let's see—I don't know."

"What do you have in your hand?" (spoon)

"Whiskey"—(laughs) "I come pretty close to it—yet."

"What are you eating now?" (bacon)

"Meat."

"What is that?" (apple)

"Bot—bot—I told it over there once—I don't know what is now."

"What are you eating now?" (bacon)

"Uh—I don't know what that man—I can't find that thread."

This loss of the names of objects is called *anomia*. You will note that his response is "I don't know." When an aphasic cannot say certain words it may be that the trouble is one of enunciation, in which case the patient will protest that he knows the word but cannot say it. In the present instance the names are forgotten. It is a very common symptom of aphasic patients. Names are symbols of objects which we use in speech and anomia is only a part of a more general disturbance of symbolic representation. We can show this by testing his power to calculate. We begin with a simple addition of 365 and 421. He adds 6; "see, this goes over and over"; puts down 8, then scratches it and adds 9; he then says "six" but puts down 7 and arrives at the sum of 796. We try him again with 342 to add to 537. He adds $7 + 2 = 9$; says "four plus three are seven" but writes a 9 and then changes it to an 8; and $5 + 3$ he adds again 9. Perseveration is evident. It is useless to insist; he cannot make more complicated additions and is totally unable to multiply or divide.

We have noted that he is unable to say many things and we can convince ourselves that this inability is not wholly to be accounted for by loss of vocabulary if we test his ability to repeat.

cat

"cat"

nose

"hose—dog—"

dog	"dog"	eye	"eye"
nose	"nose"	cat	"cat"
nose	!!!	nose	"no— dog— can't make it"
eye	"eye"	hand	"hand"

The phenomenon of *perseveration* appears again. And now we can perhaps demonstrate something quite peculiar to aphasics. I ask him to repeat after me the familiar song, "My country 'tis of Thee." He is totally unable to do so but when I ask him to sing it he does so spontaneously and correctly. Whatever he is able to say is articulated correctly. The inability to speak when the names of objects are retained (as proved by writing or otherwise) and spoken language is understood (as proved by the execution of spoken commands or otherwise) is called *anarthria*. It varies in intensity from a slight difficulty causing circumlocution to an absolute inability to make anything except inarticulate sounds. This symptom rarely occurs alone but is usually associated with aphasic troubles as in our patient.

To complete our examination we might have the patient write. He is unable to write anything spontaneously except his name but can copy simple words either in script or print. He has in other words an *agraphia*.

The disability of speech which this patient has was formerly spoken of as motor aphasia and the incomprehension of speech as sensory aphasia. But in our patient the auditory acuity and range is normal, and the visual acuity is normal although there is a homonymous defect in the visual fields. Moreover there is no auditory or visual agnosia except for symbols. If I jingle behind the patient a bunch of keys and ask him what the noise is he answers "metal." If I ring a bell he says "church." Whistling is correctly interpreted. Allowing for his paraphasia and loss of vocabulary it is obvious that he interprets correctly simple noises. If we place before him a group of small balls of colored yarns he cannot name the colors but matches them quickly and accurately. His trouble is not with sensation but with the interpretation of symbols.

But we must not get ourselves mixed up with the interpretation of the various phenomena which we have observed. We will simply remark that, although our patient has lost much of his acquired knowledge, is seriously handicapped in the solution of new problems, and his intelligence is seriously impaired, his personality is to a certain degree intact. His wife remarks that he is "only the shadow of his former self"

and yet he is tidy, never profane, always courteous, quite conscious of his defects, and much affected by them. How different is his conduct from that of a patient with a tumor of the frontal lobe of the brain!

I would like you to keep in mind the picture of our first aphasic patient. He is listless, dejected, and weeps easily. He answers frequently "I don't know" and we have convinced ourselves that he really does not know, that he has lost a great deal of his internal speech and that his intelligence is thereby greatly reduced. Now contrast him with this next patient whom you have seen before (CASE XII). He walks in with a decided limp because he has a right spastic hemiplegia which predominates in the face and arm. A large tumor was removed from the left posterior frontal region. Note that he is alert, eager, smiling and that his eyes sparkle with intelligence. He is a veterao of the great war.

"How do you feel this morning?"

"Fine."

"How long is it since your operation?"

"Ugh—ugh—fine—ugh—ugh—doggone!"

"Do you know what you wish to say?"

(Nods his head vigorously) "Fine."

"Where did you enlist in the army?"

"Winnipeg."

"What state is Winnipeg in?"

"State of— (snaps fingers)—gosh—gosh" (snaps fingers again)—
"doggone—cao't say."

"Ontatio?"

"No."

"Manitoba?"

"Fine."

"Can you say Manitoba?"

"Mani—Maoitowa."

During this time you have noted that he makes constant facial contortions as though he could not get the words past some obstruction. We note also the repetition of the word "fine" and the ejaculation of "dog gone" which recurs frequently. He insists constantly that he usually knows what he wants to say but cannot get it out. We can readily convince ourselves that this is the actual situation. We will begin with his comprehension of speech.

"Close your eyes." Correctly done.

"Put your finger on your nose." Promptly performed.

"Put your left finger on your right ear." Hesitates a moment; then executes correctly.

The three blocks are placed before him and he is told to put the large one in his pocket, throw the medium one on the floor and give the small one to me. He does so promptly. The commands may be varied at will; he always carries them out promptly and accurately. He carries out printed commands also as well. We will show him these printed cards.

CLOSE YOUR EYES. He obeys at once.

PUT YOUR FINGER ON YOUR NOSE. You see how quickly he responds. It is the same with any other commands.

It is easy to prove that he knows the names of objects although he is unable to say them. I show him this object (spectacles).

"What is this?"

"Ugh—ugh—dog gone."

"Is it a knife?"

"No" (shaking his head).

"Is it a key?"

"No" (more emphatic shaking).

"What is it used for?" (Points to his eyes.) "Do you think it is spectacles?"

"Fine!" (nodding in approval).

It is the same with other objects. You cannot make him approve of an incorrect name. If several objects are placed before him he can indicate them correctly as their names are spoken. Yet although the names of objects, at least of common objects, are retained and his comprehension of speech is satisfactory it is easy to show that there is a defect of internal manipulation of symbols if we ask him to calculate. I write for him 397 and ask him to copy the figures. He does so at once. I then write below 489 and ask him to make the sum. After many snaps of his fingers, many "dog goes" and erasures he arrives at the sum of 7122. He can do only the simplest sums and cannot subtract, multiply or divide. He has also an *agraphia*, that is, he can write very little spontaneously although he copies fairly well.

But we need not examine him in detail. I wanted only to point out that there are at least two great groups of *aphasias*—one in which emission of speech is predominantly disturbed, sometimes called *motor*

aphasia (of Broca) and another in which loss of internal speech predominates, sometimes called *sensory aphasia* (of Wernicke). *The former is produced by lesions anteriorly situated and the latter by more posterior lesions.* Since nowadays large osteoplastic openings are made these simple facts are the most essential for treatment and no further details need be given.

We will turn now to the problem of the localization in the brain of the lesions which cause these various symptoms (359) we have been at so much pains to demonstrate (cf. Fig. 30). And first we must understand clearly that none of these symptoms occurs in isolation but always is found to be associated with others of the group if they be sought for. For example a patient with a motor aphasia of Broca has usually also difficulty in writing, also sometimes a weakness of the right lower face, but on the whole his internal speech is little altered. He executes the most complicated orders promptly. When he is asked a question he makes violent efforts to answer; the animation of his countenance and attitude shows that he understands; after vain attempts to answer he seizes a pencil to write or shows by gestures that he comprehends. If we supply him with the answer he nods his approval but is totally unable to repeat after us. Usually a patient has at his disposal a few stereotyped words, often oaths. The lesions which cause relatively pure *anarthrias* are usually thromboses of the trunk of the left middle cerebral artery and the resulting softening involves the putamen, the neighboring part of the globus pallidus and the internal capsule separating them, the anterior part of the insula and to a variable extent the neighboring subcortical parts of the frontal lobes (195). Such a lesion is always associated with a contralateral hemiplegia. Rarely a relatively isolated anarthria is caused by thrombosis of the prerolandic artery; the softening then involves the gyri on each side of the prerolandic fissure. An *agraphia* accompanies the resulting anarthria. Many cortical wounds received at war, located in or near the prerolandic fissure opposite the face-area, have produced anarthria associated with *agraphia* and contralateral facial weakness. Small metastatic tumors in the same region have been reported to cause a similar syndrome (21). All of the evidence shows that the lesion responsible for inability to externalize speech (*anarthria*, motor verbal aphasia) lies anterior to the lower extremity of the anterior central gyrus.

Sensory aphasia (of Wernicke) is a syndrome consisting of loss of comprehension of spoken and written language, inability to write and *paraphasia*.

One finds also that *alexia* (word-blindness) may exist almost alone. Such patients can write but cannot reread what they have just written. Their other aphasic symptoms are very slight and transitory, but there is a hemianopia and usually the sensory and motor findings of the thalamic syndrome when such cases are due to thrombosis of the posterior cerebral artery. *Alexia* is very evident when the region of the angular gyrus is involved but is then usually one feature of an aphasia in which *anomia* is very prominent.

Incomprehension of spoken language (*verbal deafness*) is rarely encountered alone. There is usually associated auditory agnosia for elementary sounds, and amusia. The conduct of these patients is sometimes remarkable; they have a tense hunted look and often talk excessively in an unintelligible jargon (*jargonaphasia*). The power of naming objects is retained. These patients understand fairly well what they read to themselves. They are able to use numbers well and can write fairly well. The lesions in these cases have usually been found to be softenings confined to the upper temporal gyrus or in case of war-wounds localized cortical injuries in the same region.

Anomia (nominal aphasia, amnesic aphasia) is one of the commonest aphasic symptoms and is evoked by lesions over a considerable area around the posterior part of the lateral fissure. It is part of the syndrome provoked by thromboses of the posterior temporal, angular, and posterior parietal arteries and, depending on the extent of the lesion, is associated with numerous other symptoms such as hemianesthesia, apraxia, *alexia*, hemianopia, and incomprehension of speech. The effects of war-wounds confirm this localization around the posterior part of the lateral fissure and otitic abscesses in the occipito-temporal zone (37 of Brodmann) often cause this symptom in fairly pure form.

Such relatively pure symptoms as we have just described are rare. Usually the most that one can say is that either the exteriorization of speech is mainly affected or that the loss of internal speech predominates.

Although these findings are fairly definite, generally agreed upon, and useful in the localization of cerebral softenings, in actual practice *the aphasic symptoms are often deceptive and must not be relied upon for too restricted localization in cases of cerebral tumor.* Yet experience has shown that even in cases of tumor a study of the patient's aphasic symptoms is useful. If there is predominance of anarthria, with com-

prehension intact and little loss of vocabulary, the tumor may confidently be expected to lie forward. If on the other hand there is evident anomia, poor comprehension and gross perturbation of reading and calculation the tumor lies posteriorly.

After this long but important digression let us return to our first patient. It is evident now that at operation I must have damaged seriously the posterior central gyrus opposite the arm-ateia, the superior parietal lobule and the angular gyrus. The only alternative in this case would have been to go through the supramarginal and angular gyri or still lower through the superior temporal gyrus; in either case the result-

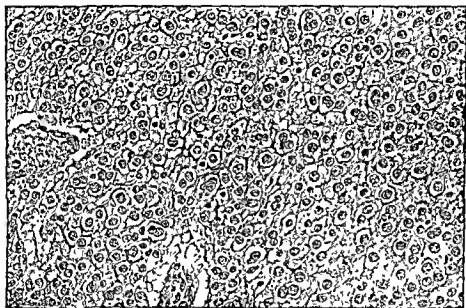


FIG. 112 Drawing of a microscopical preparation of an oligodendroglioma

ant aphasic defects would have been much more pronounced.

Although these tumors removed from the first two patients were of the relatively rare type known as an OLIGODENDROGLIOMA it must be definitely understood that *none of the symptoms we have just described is in any way characteristic of this type of tumor.* The oligodendroglioma is predominantly a tumor of the cerebral hemispheres (44) of adults and may produce any of the manifold symptoms of cerebral lesions. It has been found in the cerebellum rarely and also rarely in children. It is usually subcortical. The average age of patients when

admitted to the hospital is about forty-three years. Symptoms have been present, on an average, for five to six years before admission and patients have lived an average of more than three years after operation. Many seem to be permanently cured.

Grossly the oligodendroglioma has a firm consistency and reddish-gray color. It is rarely cystic. It often seems to have a sharp margin, but no capsule is formed. The calcified nodules can be felt with the knife when the tumor is sectioned. It is not very vascular but hemorrhages into it are frequent.

The MICROSCOPICAL STRUCTURE is quite typical (Fig. 112). The nuclei are smaller than in other gliomas and have a heavy network of chromatin. Mitoses are rare. The cytoplasm is scanty. Between the nuclei is a variable amount of fibrillary material which has often undergone a homogeneous degenerative change. Around each nucleus is often a clear halo caused by shrinkage of the cytoplasm. Each nucleus seems then to be in a little box; sometimes two or three nuclei will be found in one compartment. When impregnated specifically many of the neoplastic cells are seen to have the structure of oligodendroglia. These cells have each a small amount of cytoplasm from which a few feeble processes are given off. In addition astrocytes are commonly found and also numerous cells which form transitions between the astrocytes and oligodendroglia. Numerous cells have undergone the typical swelling characteristic of early degeneration of the oligodendroglia.

The degeneration of these tumors results in the deposition of considerable fat, and also a sort of hyalinization of the cytoplasm in which calcium-salts are deposited. In addition proliferation of the intima of the bloodvessels and calcification of their walls are common. Many nervous fibers are often seen traversing the tumor and proliferation of the oligodendroglia in the neighborhood of the tumor, especially as neuronal satellites, is frequent.

Under the microscope the oligodendroglioma most closely resembles the medulloblastoma, but its nuclei are smaller and rounder, more evenly distributed and mitotic figures are rare. The typical degenerative changes are also not found in medulloblastomas.

The preoperative DIAGNOSIS of an oligodendroglioma necessitates its differentiation from other types of glioma, especially the slowly growing varieties. It is much more commonly calcified than any other glioma, but the astrocytoma may also contain sufficient calcium to be visible in the roentgenogram.

The differential diagnosis of intracranial calcification is difficult (95). The only typical calcification occurs in Sturge-Weber disease (cf. p. 197) where the parallel curved lines are distinctive. The calcification of craniopharyngiomas in the suprasellar region is not different from that in gliomas and only its location gives it a presumptive pathological significance. When the calcification occurs near the inner table of the skull or near great dural septa one must be careful to differentiate the calcification sometimes occurring in the meninges, also the rare calcification of meningeal tumors. Any slowly growing glioma may be calcified (169) but the percentage of calcification in oligodendrogliomas is very high and usually sufficiently extensive to be visible in the roentgenogram.

The TREATMENT of oligodendrogliomas is removal by operation. They are relatively avascular, which makes their removal easier, and the postoperative prognosis is fairly good. They should always be radiated after operation, however, for they sometimes recur rapidly in an apparently more malignant form.

CHAPTER 14

GLIOBLASTOMA MULTIFORME

SYNDROMES OF THE TEMPORAL LOBE, OF THE OCCIPITAL LOBE, AND OF THE CORPUS CALLOSUM

We have seen that gliomas predominate in the cerebellum in childhood; during adult life they predominate just as definitely in the cerebrum. And about half of the adult gliomas are also of a very malignant type which is now known as *glioblastoma multiforme* because both its symptomatology and structure are very variable. It is typically a tumor of the cerebral hemispheres but may occur anywhere in the central nervous system. Tumors of this group progress rapidly and inevitably to a fatal termination. Other names by which this tumor is known are gliosarcoma, glioma sarcomatodes, spangioblastoma multiforme, neuroglioblastoma, gliome polymorphe. It has been studied extensively by Globus and Strauss. (231). We will begin our study of it with the demonstration of a typical case.

This workman (CASE XXX), forty-nine years old, had never been seriously ill until six months before admission when he began to complain of headache. Three months later he began to drag his left leg and had weakness also of the left arm and face. Later still his headaches became very severe and vision failed rapidly. There had been no vomiting.

When admitted he was very dull and uncoöperative. Vision of the right eye was reduced to 0.6 and of the left to 0.8—4. Both optic discs were badly choked with numerous hemorrhages. There seemed to be a left homonymous hemianopia, but the patient did not coöperate well enough to examine the visual fields in detail. The left pupil was larger than the right. There was a left spastic hemiparesis including the lower face. Sensory examination was unsatisfactory. The left abdominal and cremasteric reflexes were greatly diminished. He was disoriented and did foolish things; he got out of bed one evening, turned the water on in the bathroom and let it flood his room. General examination and roentgenogram of the head were normal. The clinical impression was that there was a large rapidly growing subcortical tumor in the right cerebral hemisphere.

A right osteoplastic exploration was made. The dura mater was tense and when it was opened the brain bulged markedly. The surface of the brain was very vascular and the convolutions flattened. An exploring needle met resistance everywhere a short distance under the surface. Smart bleeding followed withdrawal of the needle. It was concluded that the tumor was an extensive inoperable subcortical glioma. The bone-flap was removed and the wound closed. Next day he was quite clear mentally and completely oriented. The hemiparesis also rapidly receded. He was discharged a month later. At this time the left

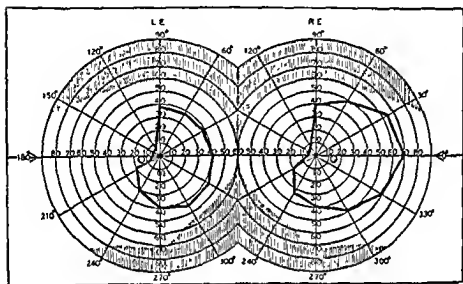


Fig. 113. Visual fields from CASE XXX.

hemiparesis was somewhat less, the choked discs had subsided, headaches ceased, and he was feeling quite well. A series of roentgen-radiations was begun and continued at regular intervals. About a week after his discharge he had a fainting-spell associated with a nauseating odor which lasted only a few seconds and disappeared. He now remembered having had such attacks before his operation. His vision was much blurred. The weakness of the left arm and leg slowly increased. He now complained also of numbness and tingling in the left arm and leg.

He returned to the hospital three months after discharge complaining of headache and weakness. The decompressed area was bulging

but soft. There was a bilateral secondary optic atrophy but no choking of the optic discs. There could now be demonstrated a left homonymous upper quadrantic defect in the visual fields (Fig. 113). There was also a left hemiparesis with spasticity, and a left hemihyesthesia predominating in the hand and forearm. Mentally he was quite clear. The old wound was reopened. The temporal lobe was very soft and necrotic. A large part of it was removed. There was evidently considerable tumor also above the lateral fissure but it was not so necrotic and very vascular; so the attempt to remove it was abandoned. The patient recovered but has an almost complete left hemiplegia as you see.

The clinical course of this patient is fairly typical of this type of glioma—the early onset of headache, the rapid development of hemiparesis, the evidences of widespread invasion of the brain, the rapid recurrence of symptoms after decompression, the relative inefficiency of roentgen-radiation are all characteristic. He will probably not live longer than a few months. The hemiparesis which developed as a result of the invasion of the tumor is familiar to us (cf. p. 163); there is no need to discuss it. But two symptoms should attract our attention, namely, the upper homonymous quadrantic defect in the visual fields and the peculiar fainting attacks. In this case the invasion by the tumor has been too extensive for us to be sure of their significance. We must, in order to understand them, study another patient in whom these symptoms are not complicated by a hemiplegia.

This man (CASE XXXI) will serve our purpose. He is thirty-six years old. His illness dates to about eight months ago when he began having spells of dizziness. During these attacks he felt as though he were falling, but never actually fell. At this time he said that while playing in the band he often played music which was different from that of the other players. This caused so much difficulty that he had to give up playing. During this time he had attacks in which he felt as though things were fading away from him. At the same time he smelled a bad odor. He felt also that his memory had been poor. For the six weeks prior to admission his vision had been gradually failing, and he had had severe frontal headaches.

He was admitted to the hospital three months after the onset of symptoms. Examination revealed marked tenderness to percussion over the left frontal and the left temporal regions. Gross examination of the visual fields suggested a defect of both right upper quadrants; the patient was too ill for detailed study. Ophthalmoscopic examination

revealed choked discs of two diopters elevation in the right eye and four in the left. There was a definite right facial weakness and a paresis of the right side of the palate. There was a weakness of the right upper extremity which was not marked and a slight increase in the tendon-reflexes of the right arm. The right knee-jerk was brisker than the left. The patient had very obvious difficulty in naming objects, in giving his own address, in telling where he worked, and also in finding the words necessary for ordinary conversation. A diagnosis was made of tumor in the left temporal lobe, probably a malignant glioma.

He was operated on the morning following admission. The gyri of the temporal lobe were found to be of three or four times their usual width and very pale. A needle was inserted in the first of these and at a

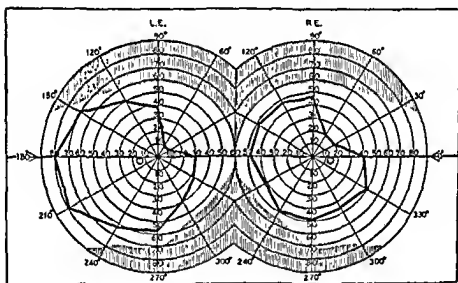


FIG. 114. Visual fields from CASE XXXI.

depth of 3 cm. a cavity was entered and a large quantity of dirty yellowish fluid was found. The cortex was then incised down to the cyst and the contents evacuated. A decompression was made in the left temporal region. The patient recovered promptly. His aphasia rapidly disappeared and also the weakness in his right hand. He was discharged nine days after operation. He returned frequently to the out-patient department and made excellent progress, except for an occasional fainting-attack accompanied by a bad odor. But after two months it was noted that his decompression had begun to bulge slightly. A month later an

attempt was made to puncture the cyst with a lumbar-puncture needle but the fluid was too thick to run out, so he was readmitted to the hospital for an attempt to evacuate the tumor. At this time his fainting-attacks had become slightly more frequent and his aphasia had again returned. There was a choked disc of two diopters in each eye. At this time careful examination of the visual fields revealed a definite tight homonymous upper quadrantic defect (Fig. 114). The old wound was reopened. Only small ragged cavities were found and much solid tumor, a large mass of which was removed with an electric scalpel.

Immediately after operation his condition was somewhat improved, but two days later he became unresponsive, had clonic spasms in both legs, and paroxysms of silly laughter. His respirations were irregular and occasionally became very deep and sighing. However, these symptoms soon disappeared and were thought to be hysterical. Subsequently he was much better, but seemed somewhat lethargic. His decompression bulged more and more and he had severe headaches. Intravenous hypertonic solutions, which had relieved his condition previously, were no longer effective. A diagnosis of postoperative hemorrhage was made and the patient taken to the operating-room where an incision in the operative field revealed a large mass of clotted blood and necrotic tissue. This was removed and a drain inserted. Subsequently the patient's condition has continued to improve. His aphasia and right-sided weakness are much better but he has now a complete right hemianopia. He is up and about. Although the decompressed area is bulging, he feels quite well.

The tumor in this instance was found definitely within the left temporal lobe. The aphasic symptoms are consistent with this localization of the lesion. No attempt was made to extirpate the tumor at the first operation for fear of aggravating the aphasic symptoms. Of course without postmortem examination it cannot be asserted that the tumor is confined exclusively to this lobe but the presumption is in favor of such a localization. The hemiparesis could be explained by pressure inward on the corticospinal tract. The hallucinations of smell occurred early and the hemianopia has been permanent; they are, therefore, doubtless due to direct involvement of the nervous tissue. This conclusion is consistent with what we know of the structure and function of the temporal lobe.

Homonymous hemianopia or, to be more accurate, a homonymous upper quadrantic defect in the visual fields which tends to progress to a complete homonymous hemianopia is one of the most frequent symp-

ions of TUMORS OF THE TEMPORAL LOBE. Its production is explained by the course of the visual radiation (Fig. 27) which loops far forward around the inferior horn of the lateral ventricle with its fibers widely scattered. A tumor developing within the temporal lobe, except for its very tip, readily involves these fibers and since they are so widely separated the early invasion of the radiation will produce only a partial interruption. It is often necessary for the demonstration of the defect to employ all the refinements of quantitative perimetry, but the value of the result justifies the time and trouble involved.

Often the patient is unconscious of the alteration of his visual fields and rarely comes to the physician complaining of visual defect. The most frequent symptom of which the patients complain is an epileptic fit of some sort. It is not uncommon for the illness to be initiated by a generalized convulsion. Later on, or even without a preceding generalized attack, peculiar minor attacks occur. In their mildest form they consist of so-called *dreamy states*. Even the most intelligent of patients exhausts his vocabulary in attempting to describe what occurs. Those who watch such attacks note that suddenly the patient ceases to talk or move, his eyes stare into space, a blank look comes over his face, and after a few seconds he resumes his activities. The patient himself, if capable of introspection and description, reports that a *feeling of unreality* comes over him, the surrounding world seems to fade away, although he remains conscious of it, and he cannot speak. Various changes appear to occur in surrounding objects; they usually seem vague and indistinctly outlined, but may occasionally appear unusually beautiful or even to change in size. Less intelligent patients report only that they feel "queer" and the significance of the attacks might be overlooked were it not that they were accompanied often by other phenomena more easily described. Prominent among the latter are *hallucinations of smell and taste*. Accompanying the dreamy state, or independently, the patient is conscious of a wave of odor, either pleasant or unpleasant, which lasts but a few seconds and passes quickly away. At the same time, or again independently, there may be present in the mouth a peculiar taste which is also transitory. The patients often make concomitant smacking movements of the lips. These phenomena have long ago been shown to be due to invasion of the uncus by the tumor and hence are known as *uncinate fits*. Often in association with the uncinate fits occurs another significant phenomenon. The patient may see usual objects or scenes such as faces, people playing cards, little women

walking, etc., on the side of the defect in his visual fields. The apparitions are called *visual hallucinations* and may occur without an accompanying uncinat attack. Rarely *auditory hallucinations* occur, such as noises, whistling, the tinging of bells, etc., preceding or accompanying the attack. Such preliminary sensory phenomena are called *aurae*.

The dreamy state, the hallucinations of smell or taste, the visual hallucinations or the auditory hallucinations may be in the later stages of the illness preliminary to a convulsion which begins with turning of the eyes and head to the opposite side, tonic contractions of the limbs, usually generalized, and loss of consciousness.

We have already discussed aphasia in detail. Incomprehension of speech, even auditory agnosia, paraphasia, rarely jargonaphasia have been observed. In cases of tumor of the temporal lobe the most frequently observed symptom is anomia. This is probably due to the fact that few gliomas are confined strictly to the temporal lobe and we know that the extension of any sort of lesion backward toward the parietal or occipital regions is accompanied by anomia and alexia which masks to a certain extent the symptoms of involvement of the purely temporal regions. Aphasic symptoms, of course, point almost invariably to involvement of the *left* temporal region.

To the nucleus of peculiar epileptic fits and defects in the visual fields (also in part the aphasia) are added, as the tumor expands, other symptoms from involvement of neighboring regions. Many of the aphasic symptoms come into this category, for example alexia. Prominent also are symptoms of involvement of the corticospinal tract, most frequently evidenced by a lower facial weakness on the contralateral side which may be visible only on emotional stimulation. Less frequently the weakness first appears in the contralateral leg. One may find also a contralateral extensor plantar reflex, absence or diminution of the abdominal reflexes and, if the disease is allowed to progress long enough, a contralateral hemiplegia. The customary primary involvement of the face is probably to be explained by pressure upward on the lower end of the anterior central gyrus where the fibers arise which innervate the face, whereas when the leg suffers first the tumor has probably extended deeply and pressed upon the peduncle or internal capsule in which the fibers innervating the leg lie most laterally. The paralytic symptoms at first are present only transitorily following epileptic attacks. Rarely extrapyramidal rigidity may occur from pressure upon the basal ganglia.

Mental symptoms, apart from the aphasia, are not uncommon. Most frequently noted is defective memory. We may suspect that this symptom is not always differentiated from the loss of vocabulary which occurs with the aphasia. There is no question, however, that pressure or extension of the tumor into the frontal lobe may cause those changes in character and personality which are seen in cases of glioma confined to the frontal lobes alone. These symptoms are often due also to obstruction of that portion of the blood-supply of the frontal lobe which comes from the sylvian vessels.

One other uncommon but characteristic sign of tumors on the inner surface of the temporal lobe is paresis of the homolateral third nerve. Perhaps some of the early ocular signs must be explained by pressure on sympathetic fibers, causing a myosis and slight ptosis of the upper eyelid. Later the myosis changes to mydriasis, the ptosis is exaggerated, and a downward and outward squint may occur—the classical appearance produced by paralysis of the oculo-motor nerve. The other cranial nerves are rarely involved. Anosmia is uncommon, optic atrophy does not occur, weakness of the external ocular muscles is rare and involvement of the fifth nerve is confined to an occasional weakness of the homolateral corneal reflex. One might expect deafness, not from involvement of the nerve but from destruction of the cortical auditory area. Although diminution of auditory acuity in the contralateral ear has been occasionally reported, it is relatively inconspicuous and few accurate studies have been made.

Sooner or later of course, headache, vomiting and choking of the optic discs occur. These symptoms of increased intracranial tension are not peculiar to tumors of the temporal lobe. The choking of the optic discs is rarely higher or earlier to appear on the side of the tumor; vomiting seems to be often accompanied by nausea; the headache is not localized to the temporal region and there is rarely tenderness to percussion or pressure over the tumor.

The localizing diagnosis of tumors of the temporal lobes is not so difficult since quantitative perimetric examinations are regularly made. Tumors of the tip of the temporal lobe may be confused with tumors of the frontal lobe. In these latter cases the visual radiation may escape, a weakness of the contralateral lower face occur (as with tumors of the frontal lobe) and changes in personality and intelligence be prominent. Careful search for some aphasic defect, and inquiry into the nature of possible fits will usually establish the correct temporal

localization but rarely it may be impossible when the patient is first observed. Temporal tumors may be confused also with cerebellar tumors but this error should rarely occur. If one remembers that cerebellar tumors are rare in adults (acoustic tumors apart), and is on his guard, it is almost always possible to make the correct diagnosis. In those cases which have come under my observation the cerebellar localization was made on really inadequate grounds. Most frequently the confusing symptom observed is nystagmus. A fine tremor of the hands is occasionally found, either homolateral, heterolateral or bilateral, but asynergia, hypermetria, typical reeling gait, and hypotonicity I have never observed.

The greatest difficulty is to differentiate gliomas of the temporal lobes from those of the occipital lobes. Certain symptoms of tumors of the temporal lobe are rarely, if ever, produced by tumors of the occipital lobe—such as uncinatate fits, facial paresis, oculomotor palsy—but when these symptoms are absent one is never sure whether they are missing because the tumor is in the occipital region or whether they simply have not been produced by the temporal lesion. One then has to fall back on nuances of the symptoms and signs common to both, namely defects in the visual fields, visual hallucinations, aphasia and epileptic fits. Gliomas are rare in the occipital lobe and I have no patient with a tumor confined to the occipital lobe to demonstrate to you, except a young girl who was completely blind when she came to us, but the following case is important in this connection and the brain is interesting for you to see.

A salesman (CASE XXXII), 44 years of age, began three months before admission to have difficulty in making out his reports because of inability in understanding written language. He could not grasp the meaning of a word until it was spelled for him. This made him irritable and disagreeable. The difficulty increased until a month later he was unable to read at all, lost his memory for recent events and was often completely disoriented. He was much depressed and wept frequently. He soon began to suffer from headache, at first intermittent and not severe, but about two months after onset it became much worse and a week later was associated with projectile vomiting. He became completely disoriented and talked incoherently. He seemed not to see things on his right side. Finally he became so agitated that he was brought to the hospital.

When admitted he was very restless, did not seem to recognize

anyone, and called continually for his "Aunt Fanny." He used many other words but in incoherent fashion. He gave no attention to questions. The optic discs were choked to 3-4 diopters. There was a slight right facial weakness, but no other signs of hemiparesis. Sensory examination was impossible, also examination of the visual fields, because of his agitated and uncoöperative state. Because of the history of early alexia and difficulty of seeing to the right a diagnosis of tumor in the neighborhood of the left angular gyrus was made.

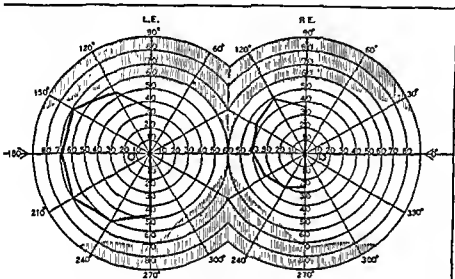


FIG. 115 Visual fields from CASE XXXII

A left osteoplastic exploration was carried out under ether-anesthesia. The brain was under great tension and bulged markedly when the dura mater was opened. A subcortical tumor could be palpated under the region of the supramarginal and angular gyri. Puncture in this region met resistance about 2 cm. under the cortex and bleeding followed withdrawal of the needle. The tumor was judged to be inoperable. A subtemporal decompression was made, the boneflap replaced and the wound closed. The patient recovered promptly and within two days could answer questions in well-formed complete sentences. He still wept often because he could not recall many things. Roentgen-radiation was begun and two weeks later he was discharged. At this time he was still completely unable to read and could not write. He could, however, distinguish colors. Comprehension of spoken lan-

guage was good. He had much difficulty in recalling names of objects and persons. He was oriented, his memory was much better and he was quiet and less emotional. The choking of the optic discs had completely disappeared and it could be determined that he had a right homonymous hemianopia (Fig. 115). There was also distinct loss of sense of position in the right hand. Roentgen-radiation was continued. A month later he was feeling very well, in fact a little euphoric. He talked a great deal and without error in speech. His memory was now clear.

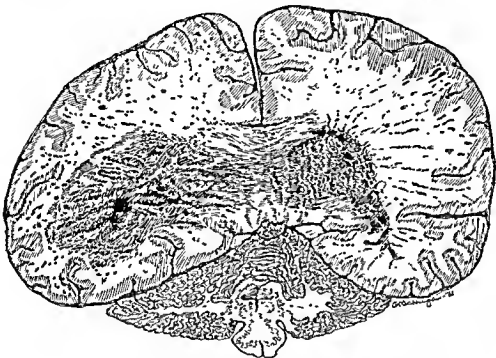


Fig. 116. Cross section of brain from CASE XXXII. The tumor extends through the splenium of the corpus callosum into both hemispheres

He was still unable to read. He could write, but was unable to read afterward what he had written. There was a complete right homonymous hemianopia including the macula. He had no headache and the decompressed area was only slightly bulging. About a month later still he suddenly became stuporous following a roentgen treatment and the decompressed area became tense and bulging. He was thereafter very aphasic, unable to understand, and talked with incorrect and jumbled words. He was completely disoriented; could not even remember the way to his room. There was no paralysis of his limbs. He gradually declined and died three months after operation.

A complete necropsy was made half an hour after death. General examination revealed little of interest except a bilateral terminal bronchopneumonia. In examining the brain we find a tumor involving the splenium of the corpus callosum and extending backward into both occipital lobes (Fig. 116). It is much more extensive in the left hemisphere and has grown laterally into the region of the angular gyrus. The tumor contains numerous necrotic and hemorrhagic areas. Further examination by serial sections stained with Weigert's method shows that the tumor extends back into each occipital lobe as far as the tip of the posterior horn of each lateral ventricle, which is about 2 cm. anterior to the tip of the occipital pole on either side. The tumor in the right hemisphere has pushed the lateral ventricle upward and outward but has not obliterated it and the tumor has not invaded the brain lateral to it. On this side the optic radiation is clearly visible. On the left side the tumor has obliterated the ventricle except for the most posterior extremity of the posterior horn which is filled with coagulum and is slightly dilated. Anteriorly the tumor has invaded the subcortex on the lateral side of the ventricle and interrupted the optic radiation. It approaches nearest to the cortex of the angular gyrus, but even here stops more than 1 cm. short of the cortex. Near the posterior border of the supramarginal gyrus the tumor curves medially through the splenium.

It is of interest to note that once the intracranial tension had been reduced *the aphasic symptoms in this case were practically confined to an alexia*. Most of the cases of relatively pure alexia have been due to occlusion of the posterior cerebral arteries. The tumor in this instance lay almost exclusively in the territory supplied by the two posterior cerebral arteries. It did, however, invade beyond this area just underneath the left angular gyrus. The alexia might, therefore, be explained by involvement of the projection-fibers of this gyrus.

The optic radiation, of course, extends to the tip of the occipital pole so it should occasion no surprise when I tell you that the most constant signs of TUMOR OF THE OCCIPITAL LOBE have to do with it. Rare indeed is the case in which either visual hallucinations or defects of the visual fields are absent. When hallucinations are absent the diagnosis is rarely made until such defects appear. *The hallucinations differ from those caused by tumors of the temporal lobes in that they consist of unformed visual phenomena*. The patient sees flashes of light, stars, streaks, lightnings, either preceding convulsions or isolated. These

phenomena are usually seen on the contralateral side but are sometimes said to be directly in front of the patient. Any addition of formed objects to the hallucinatory visions indicates extension of the tumor into the temporal region. Auditory hallucinations may then also appear.

The defects in the visual fields vary, but are always of a homonymous form. A complete hemianopia is usually present when the first examination is made, with or without sparing of the macula. In a considerable number of cases a homonymous quadrantic defect is found, but this is more common with tumors of the temporal lobe. There is rarely any possibility, from the visual fields alone, of distinguishing with certainty between occipital and temporal tumors. It is said that the macula is more often spared when the lesion is farther toward the occipital pole. This may be true of vascular lesions but the sparing of the macula is of little significance in cases of tumor. Other visual phenomena are alexia and visual agnosia, and very rare cases of difficulty in spatial orientation or distortion of visual images.

But it should not be forgotten that the visual symptoms and signs, although the most constant, are infrequently complained of by the patients; hence the necessity for examination of the visual fields of every patient suspected of harboring an intracranial tumor. Visual hallucinations occur in only about 25 percent of cases and patients rarely complain of symptoms referable to constriction of the visual fields. Occasionally one will remark that he runs into objects on one side or that his vision is defective on one side. The patients complain most constantly of the symptoms of increased intracranial tension, in no wise different from those due to tumors anywhere in the intracranial cavity, and of epileptic attacks. The latter vary from minor attacks (sometimes accompanied by visual aura) without loss of consciousness, to major convulsions initiated by turning of eyes and head to the opposite side. Following the attacks there is sometimes transitory weakness of the side opposite the lesion, of considerable importance in lateralizing the tumor. Epileptic attacks of some sort occur in almost half the cases.

Slight hemiparetic symptoms and slight hemihypesthesias of the contralateral side are frequent and signify involvement of adjacent regions by pressure or edema. They rarely reach the intensity seen with tumors of the parietal or temporal lobes. In the left hemisphere invasion of the temporal lobe is accompanied by aphasic symptoms, essentially nominal aphasia with alexia and visual agnosia. It should

be remembered that the occipital lobe is very small so that tumors confined to it are rare; they almost always involve also the parietal or temporal lobes or both.

Confusion with tumors of the cerebellum may occur if the patient be blind. Most commonly observed is a nystagmus, rarely if ever true cerebellar asynergia, and if only one remembers that in these cases nystagmus along with paresis of the sixth nerve and mental confusion almost invariably occurs concomitantly with high intracranial tension, he will be on his guard and rarely be drawn into error.

We have seen that the tumor in the last case invaded the splenium of the corpus callosum and this raises the question of the functions and symptomatology of this interesting structure. But before discussing this problem we may study another tumor which involved the rostrum of the callosal body. And I should like to draw your attention also to the frequency with which these malignant tumors pass from one cerebral hemisphere to the other along this great commissure.

The patient (CASE XXXIII), 57 years old, had been a successful business-man and well, except for a gastric ulcer relieved by gastroenterostomy. Three months before admission to the hospital he vomited and complained of feeling hot, but continued to work. A week later his associates noted that he acted "queer." His wife was called to him and found him stupid and drowsy, going to sleep readily in the daytime, rather restless at night, dull mentally, taking little interest in anything, confused, and disoriented. He vomited several times. He was taken to a sanatorium where he was still disoriented. He mistook strangers for old friends. He was confused and indifferent and had no insight into his condition. His memory for recent events was poor. His bloodpressure was 124/82 and his pulse-rate 72; there was no evidence of cardiovascular disease. His speech was normal. No paralysis or loss of sensation was found. There was no choking of the optic discs at that time. A lumbar puncture obtained clear fluid, containing 5 cells per cu. mm.; the Wassermann reaction on this fluid was negative, the globulin increased and the gold-curve 3455440000. His condition changed little during the next month. Then one day he reeled while walking and almost fell. He was put to bed. The next morning he vomited and collapsed; the pulse became very weak and rapid and his temperature rose to 40°.

When admitted to the hospital his temperature ranged between 38° and 40°. He lay in bed in a stuporous condition, did not speak

and swallowed with difficulty. The temporal arteries on both sides were distended and tortuous. The eyes were rather constantly deviated to the left. The optic discs were perhaps slightly choked. There was a constant spontaneous nystagmus, with the quick component to the left, and possibly slight weakness of the left side of the face. Generalized fine clonic twitchings of the musculature were present over the entire body. Both arms could be moved spontaneously. The abdominal reflexes were absent. The tendon-reflexes were present but weak; flexor

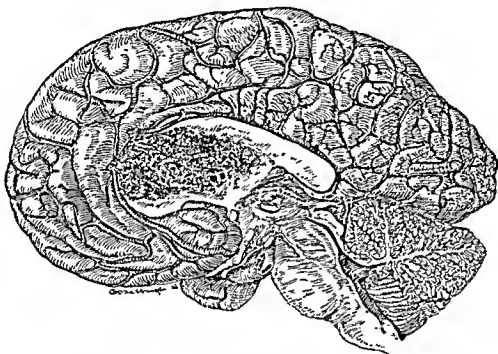


FIG. 117. Median section of the brain from CASE XXXIII. Tumor destroys the rostrum of the corpus callosum and extends laterally into both frontal lobes.

plantar reflexes were obtained on both sides. Pin-prick was apparently felt everywhere. The neck was slightly stiff. Respiration was irregular and there were periods of auricular fibrillation. He was given digifolin and several intravenous injections of normal saline solution. He improved slightly and said a few monosyllabic words. It was obvious, however, that he did not know how to use his hands and, moreover, there seemed to be also an apraxia of the facial and faucial musculature because when food was placed in his mouth he made useless contortions of the mouth and tongue, rolling the food around aimlessly.

He seemed to want to eat but always ended by spilling the food. A roentgenogram showed the sella turcica to be greatly eroded, the floor and dorsum not being visible. The clinical impression was tumor of the frontal region of the brain, probably involving the corpus callosum. A bad prognosis was given. To confirm our opinion air was injected into both lateral ventricles. Roentgenogram then disclosed that the right ventricle was constricted in the neighborhood of the optic thalamus. The anterior horn of the left ventricle was not filled. The results of the injection of air were interpreted as confirming the clinical diagnosis. A right subtemporal decompression was then made under local anesthesia as a preliminary to roentgen-radiation, but he rapidly declined and soon died.

A postmortem examination revealed nothing of general importance except bilateral adhesive fibrous pleuritis and acute hypostatic edema, hyperemia and bronchopneumonia of both lungs. In the brain we find a tumor involving the corpus callosum from the knee backward for 4 cm. (Fig. 117). It extends laterally into both frontal lobes, completely occluding the anterior horn of the left ventricle. The anterior horn of the right ventricle and the posterior portions of both ventricles are dilated. The third ventricle is flattened from above. On the external surface the convolutions are flattened only in the frontal region. The frontal lobes are markedly swollen with smooth shining surfaces. The optic nerves are flattened and the optic chiasm pushed backward and downward against the stalk of the hypophysis which is compressed and adherent to the tuber cinereum. The dorsum sellae had been completely resorbed.

The CORPUS CALLOSUM is an enormous commissure connecting the two cerebral hemispheres. The exact origin and termination of its fibers in the cortex are not definitely known but they join mainly homologous areas. Experimental studies have added little to our knowledge of this structure. The most common symptom following transection in animals has been lethargy. Considering the high mortality it is not surprising that the few survivors are somewhat lethargic. Electrical stimulation of the middle portion causes muscular movements. About the only definite lead one gets from experimentation has been the demonstration that a dog whose corpus callosum has been transected is no longer able to localize sounds, and study of conditioned reflexes also indicates that the callosal body is important for the bilateral synergic activity of the hemispheres.

The corpus callosum has been sectioned at operation on numerous occasions with surprisingly little disturbance in normal persons (4). It is, of course, incredible that such a massive accumulation of nervous fibers should have no function. For the study of the clinical symptomatology of this structure thromboses of the anterior cerebral artery are most illuminating (113). The resulting softening causes a crossed hemiparesis predominating in the leg as is well known. But when the callosal artery is occluded the resulting softening of the major part of the corpus callosum sometimes adds to the clinical syndrome an apraxia of the left hand, on whichever side the hemiparesis may be.

Three varieties of apraxia are usually distinguished—motor, ideomotor, and ideational. The ideational form occurs in any profound dementia and as such is seen in amnesic aphasia. A bilateral ideomotor apraxia accompanying a global aphasia has been often described in lesions of the left supramarginal gyrus and the subjacent white matter (76). The motor type is always unilateral and affects the left hand in right-handed people. Voluntary acts cannot be performed, whereas involuntary gestures are possible. It is often accompanied by forced grasping in the affected hand and by hemiparesis of the right side. This motor type of defect is that which accompanies occlusion of the callosal artery (465).

Section of the corpus callosum rarely causes such an apraxia because few persons are strongly left-brained for motor acts other than speech and such activity can usually be initiated from either hemisphere, nor should section of the corpus callosum be expected often to cause aphasic disturbances except in those rare persons who have a dominant right occipital lobe associated with a dominant left temporal lobe.

If the functions and relationships of the corpus callosum are so imperfectly understood it can cause no surprise that the diagnosis of its tumors is difficult. From time to time clinicians have tried to determine a characteristic syndrome but *each new attempt seems more obscure than the last* (8). Most of the symptoms described cannot be distinguished from those due to involvement of neighboring parts of the hemispheres, nor is there any reason to suppose that they could, since the corpus callosum is a large commissure connecting these regions. Tumors in its anterior part cause mental symptoms differing only quantitatively from those we have described as characteristic of tumors of the frontal lobes. Some of the most profound dementias accompany these tumors. Apathy, drowsiness, and defective memory are the symp-

toms most often mentioned. These symptoms may be pronounced in the absence of greatly increased intracranial tension. Motor defects are frequent. They usually predominate in the legs and one side is almost always more involved than the other. Before the pyramidal signs become definite there is sometimes an unsteady gait, unaccompanied however by nystagmus, hypermetria, asynergia, or other signs of involvement of the cerebellum. Sensory defects are uncommon. Paralysis of the cranial nerves are absent, except sometimes of the abducens when the intracranial tension is high. Epileptiform convulsions, tremor, and choreiform movements may occur.

When a progressive mental deficit develops, accompanied by a hemiparesis and slight motor disturbance also on the other side, without sensory disturbance and without aphasia, before signs of increased intracranial tension have become marked, a tumor of the corpus callosum may be suspected. If the spinal fluid is yellow and its content of cells increased, indicating the approach of the lesion to the ventricular walls, the diagnosis is more certain. In those rare cases in which a unilateral motor apraxia can be demonstrated the diagnosis becomes sure.

Aside from tumors of the frontal lobes, tumors of the callosal body are most often confused with cerebral arteriosclerosis or presenile dementia. The differentiation may be impossible before symptoms of increased intracranial tension appear and study of reported cases indicates that these diagnoses are very often made in the early stages of the disease. General paresis is also often suspected but more readily ruled out. That these tumors should be confused with those of neighboring parts of the brain should occasion no surprise when it is realized that *the rare unilateral apraxia is the only characteristic clinical symptom and that tumors are rarely confined to the corpus callosum*. I am sure, however, that they should rarely be mistaken for tumors of the cerebellum. There is usually observed an unsteady gait without nystagmus and without incoordination of the upper limbs, simulating the syndrome of the vermis. Such a syndrome from cerebellar tumor is exceedingly rare in adults. Cerebellar tumors in adults are almost always accompanied by dysmetria in the upper extremities. The mental obfuscation is due to increased intracranial tension and may be made to disappear by an intravenous injection of hypertonic saline solution, whereas the profound mental deficit of callosal tumors is not affected.

Finally I should like to relate two cases which show that the gli-

oblastoma multiforme may run its course without any signs of intracranial hypertension. We have already learned that there are some types of intracranial tumor, such as the pituitary adenoma, which rarely increase the intracranial tension, and increasing numbers of tumors are being operated on before the intracranial tension becomes high (482) but it seems not to be appreciated how commonly *even the most malignant gliomas may run their courses without producing the classical triad of headache, vomiting, and choked discs.*

A housewife (CASE XXXIV) of forty-eight, who had always been well except for a pelvic repair, began ten months before admission to have attacks lasting only a few moments during which she felt faint, smelled a most nauseating odor, and felt a numbness in the right side of the face, sometimes also in the right arm and leg; she did not lose consciousness. She became increasingly forgetful and irritable. Sometimes she misused words. Two months after the onset of these troubles she began to complain of frontal headache. Finally she collapsed one day while on a shopping-expedition and was brought to the hospital.

On admission there was a lower right facial weakness, especially evident on emotional stimulation. The tendon-reflexes were slightly exaggerated on the right side. Possibly there was also some slight hypoaesthesia to pain and temperature on the right half of the body and at times slight difficulty in naming objects. The optic discs were normal; she did not cooperate for careful examination of the visual fields. There were no evidences of lues or cardiovascular disease. A roentgenogram of the skull was normal. The clinical impression was of early tumor of the left temporal lobe.

A left osteoplastic craniotomy therefore was performed. The brain was not tense. A subtemporal decompression was made. An exploring needle met resistance as from a tumor at a depth of 4 cm. under the surface of the temporal lobe. The tumor was judged to be inoperable and the wound closed. The patient remained after the operation for several days in a sort of cataleptic stupor. She seemed to be peacefully sleeping. The bloodpressure and pulserate were normal and the decompressed area not tense. She did not talk but would open the eyes, put out the tongue, or squeeze the hand on command. The right arm and leg seemed weak. It was not until two weeks later that she began to arouse. She was given a suberythema-dose of roentgen-radiation and discharged with what seemed to be an almost complete motor aphasia

and a right hemiparesis. She improved steadily for about a month, was walking around the home and speaking fairly well and then began steadily to decline. Two months later she was bedridden, completely irresponsive, a blank expression on her face, incontinent, and with a right hemiplegia. The decompressed area was perfectly flat; it never bulged at any time during the course of her illness. No further radiation was advised since some doubt was felt concerning the diagnosis, and a few days later she died.



FIG. 118. Cross section of brain from CASE XXXIV. Tumor destroys the left island and extends downward into the left cerebral peduncle.

A postmortem examination was restricted to the head and disclosed, as you see (Fig. 118), a large tumor in the left hemisphere which has destroyed the island and extended into the internal capsule and thalamus, pushing the midline far to the right. Its cut surface is studded with hemorrhages, degenerated areas, and small cysts.

The other patient (CASE XXXV) was a middle-aged school-teacher who after a strenuous year complained of being tired but otherwise was well until one day she suddenly stopped talking, then screamed and

became stiff and trembled all over. She remained unconscious until the next morning, having in the meantime two other trembling-spells. She was then well except for occasional complaint of headache for three months when one day after dinner she became dizzy, talked somewhat incoherently for an hour or more and then had another convulsion. It began with twitching in the right side of the face and turning of the eyes to the right. She screamed, lost consciousness and thrashed about for half an hour. Since that time she had not been quite right mentally.

When she was admitted to the hospital two days after this last accident she was inattentive and disoriented. In speaking there seemed to be slightly less action on the right side of the face. The right biceps reflex was slightly more brisk than the left. Her speech was somewhat monotonous; as her sister expressed it "slow, deliberate, and halting." There seemed to be no aphasia. There was no sensory disturbance except possibly to two-point discrimination in the right hand. The right abdominal reflex was less brisk than the left. The pressure of the spinal fluid was only 100 mm. of water. There was no edema of the optic discs and no defect could be found in the visual fields. The clinical impression was tumor of the left frontal lobe, but vascular insult could not be ruled out in spite of the absence of any evidence of cardiovascular disease, so air was injected into the ventricles. No dilatation or distortion of the ventricular system was seen; the temporal horns were well filled and seemed perfectly normal. After the ventricular puncture she became mentally much clearer and spoke freely. She was discharged with the advice that she give up her teaching. The final impression was of a degenerative disease of the brain. After discharge she continued to speak normally but the sister (a physician) noted that she seemed often not to understand what was said to her, became more and more apathetic and finally died about two months later. She did not complain of headache, did not vomit, and there was never any choking of the optic discs. Necropsy revealed a glioblastoma which occupied the tip of the left temporal lobe, compressed the basal ganglia and displaced the midline slightly to the right.

The GROSS APPEARANCE of glioblastoma multiforme (232), one of the most vicious of all intracranial tumors, is one of the most beautiful when seen at necropsy. The cut surface is a kaleidoscopic display of reds, browns, yellows, grays, and greens. This appearance results from the numerous degenerations and hemorrhages, old and new, which have occurred in the tumor. These tumors are usually subcortical so

that one sees on the surface of the brain only flattening of the convolutions, which may be purely local if the tumor be near the surface, or generalized if intracranial tension has been long increased. When the tumor has reached the surface a reddish-gray area is visible within which it may be possible to trace the course of the gyri and sulci but usually they are obliterated or pushed to the periphery of the lesion and compressed. Sometimes the tumor becomes adherent to the dura mater and this fact, together with the compression of the surrounding

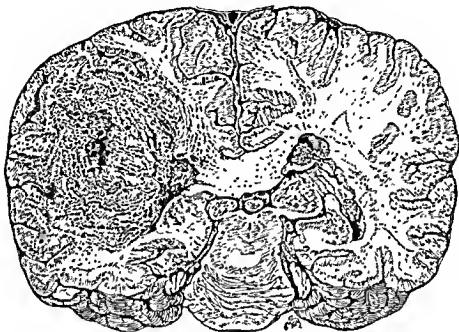


FIG. 119 Typical glioblastoma multiforme which has invaded and destroyed without much distortion of the brain.

gyri, may lead to an erroneous diagnosis of meningeal tumor until the attempt is made to dissect the tumor away from the brain. The surface of the tumor is very vascular and the bloodvessels in the neighborhood are dilated. Sections through the tumor usually disclose that it is both invasive and expansile. Many of the normal structures have been destroyed by the growth, others pushed aside. The sagittal plane is usually displaced to the opposite side. Often, however, such a tumor seems to grow almost exclusively by invasion and destruction so that the surrounding structures are barely distorted (Fig. 119). The exact margin

is marked by the increased vascularity, especially in the subcortical regions. There is no capsule, either of connective tissue or gliosis. Often in the neighborhood of the tumor is a marked edema which may be more responsible for the intracranial hypertension than the size of the tumor. When the tumor develops in the neighborhood of one of the major arterial trunks softening of the brain may result from the occlusion of its blood-supply. It seems to have difficulty in penetrating large fiber-tracts such as the internal capsule or corpus callosum.

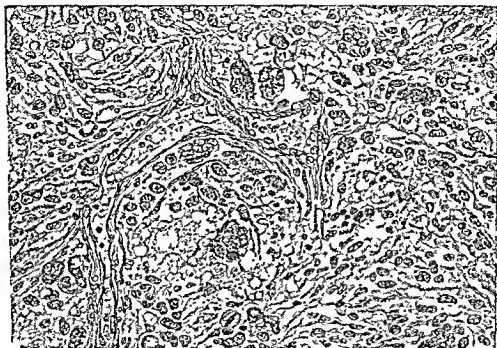


FIG. 120. Drawing of microscopical preparation of a glioblastoma multiforme.

MICROSCOPICAL STUDY reveals a bewildering series of cellular forms and appearances; hence the name of glioblastoma multiforme (Fig. 120). Most commonly the predominant type of cell is small with scanty cytoplasm and oval nucleus. Mitotic figures are numerous and many are abnormal. It is possible also that amitotic division occurs. At any rare multinucleated giant-cells are frequent and in many of them the nuclei can be seen to be connected by strands of the nuclear membrane as in the nuclei of polymorphonuclear leucocytes. In many such tumors the cells are predominantly spindle-shaped so that they were long supposed to be akin to the spindle-celled sarcomas arising from con-

nective tissue and were accordingly called gliosarcomas. These two types of tumor can, however, be readily distinguished by a careful study. The cells of the glioblastoma multiforme never form collagen, elastin, or reticulin. The connective tissue in these tumors is always confined to the walls of the bloodvessels except in necrotic areas and even here the dividing line between glioma and granulating tissue is sharp and easily seen. The nature of the neoplastic cells is clearly proved by impregnation with specific methods for the neuroglia. For this purpose absolutely fresh material and perfect technique are necessary and the impregnations must be made at a much higher temperature than is necessary for the normal neuroglia. It is then possible to see that numerous neoplastic cells resemble closely unipolar or bipolar spanglioblasts or astroblasts and that many are even abnormally developed astrocytes. The last cells are apt to be most evident near the bloodvessels and often have their bodies closely applied to the walls after the fashion of the normal perivascular astrocytes (of Andriezen).

Bloodvessels are numerous and quite abnormal in structure. For this reason the symptoms of these tumors often develop acutely from thrombosis or hemorrhage. Their walls are thin and composed of an endothelial sheath surrounded by strands of collagenic tissue. There is never a muscular sheath. The connective tissue is usually degenerating, edematous, infiltrated with fat, or hyalinized. Tortuosities and aneurysmal dilatations are frequent. Proliferation of the intima and thromboses are numerous. From such thin-walled and degenerated vessels it is understandable that numerous hemorrhages and softenings occur. It is often difficult to find an area of healthy neoplastic cells for study. The degenerated areas often lie in long streaks with the pyknotic nuclei pushed to the periphery to form pseudopalisades. The earliest degenerative change in the parenchyma of the tumor seems to be a matting together of the processes of the cells. The entire cytoplasm becomes homogeneous and appears to form a syncytium. In these areas fat is formed and numerous macrophages appear to aid in the removal of the degenerated material. These macrophages are readily demonstrated by supravital examination in a weak solution of neutral red. Their presence is an important aid in the immediate diagnosis of these tumors because they are rarely present in other types of glioma. As the tissue dies and the products of its degeneration are removed the necrotic zone is invaded by young fibroblasts and typical granulating tissue may result which later transforms itself into a collagenic scar. But in other cases exudation from the ves-

sels prevents the organization of the necrotic area and ragged cavities are formed, filled with a dark, yellowish fluid with a high content of albumen and debris of necrotic tissue. This fluid usually clots when exposed to the air. The proliferating fibroblasts do the best they can under these circumstances and attempt to form a wall of connective tissue around the cavity.

The multifarious processes of degeneration, hemorrhage, and reor-

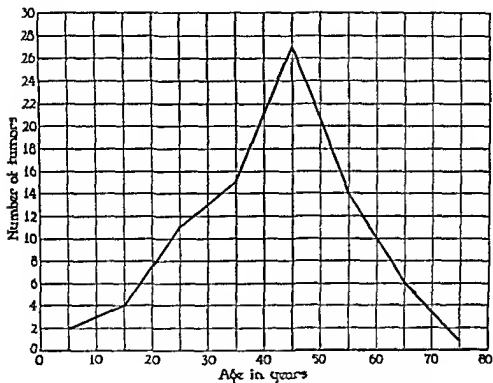


FIG. 121. Graph of age-distribution of glioblastoma multiforme

ganization which go on in the tumor, plus the polymorphous structure of the neoplastic cells, amply justify the name of glioblastoma multiforme now applied to this tumor. The margin of the tumor, difficult to determine with the naked eye, is no more definite under the microscope. The neoplastic cells invade the surrounding cerebrum and mitotic figures may be found in what appears to be normal tissue. On the other hand, neurones and particularly axones with their myelin-sheaths are often found within what is obviously neoplasm. These findings indicate

that the tumor advances by infiltrating the surrounding tissue but occasionally it increases in size faster than the infiltration, resulting in a fairly sharp margin, and compression of the normal tissue.

These tumors form a vast group which could doubtless be subdivided on morphological grounds into many subgroups, but there seems little practical advantage in doing so. One fairly well characterized subgroup has, however, been segregated in which the predominant cell-type resembles an astroblast. These astroblastomas (42) have approximately the same site of origin, age-incidence, and gross appearance, but are slightly less malignant.

The preceding records give us a rather confused, hence adequate, conception of the clinical course of this malignant tumor. No group of symptoms forms a definite syndrome typical of it. The impression of predominantly aphasic disturbances is doubtless due to the distressing nature of these symptoms, since statistics do not prove any greater incidence in the left hemisphere. It is characteristically a tumor of the cerebral hemispheres of adults, the average age of onset of symptoms being about forty years (Fig. 121). The average length of life is about twelve to fifteen months. It grows very rapidly, giving usually severe signs of increased intracranial tension within a few months. But in many cases the neurological symptoms may precede for some time the onset of pressure-symptoms and the symptoms are so often sudden in onset, due to hemorrhages and thromboses within the tumor, that the diagnosis from primary vascular diseases is difficult (183). This tumor furnishes the most striking exceptions to the general rule which we have given that intracranial tumor is characterized by a gradual progression of the symptoms. The neurological manifestations of the glioblastoma are as manifold as the physiology of the cerebrum and usually the widespread growth of the lesion makes their interpretation difficult. These tumors are, therefore, of little use for the study of the local pathophysiology of the brain. We may say that whenever a middle-aged patient, otherwise in good health, has suddenly evidence of an insult to the brain, recovers, but soon has another accident and then begins to suffer from headache, a glioblastoma should be suspected. The rapid addition of new symptoms indicating the involvement of adjacent parts of the cerebrum makes the diagnosis almost certain even in the absence of signs of increased intracranial tension.

The DIAGNOSIS must be made principally from syphilis, vascular degenerative disease, encephalitis, or rarely from degenerative paren-

chymatous degenerations of the type of presenile dementia. The differentiation of syphilis is based principally on the characteristic symptoms which this disease provokes in the nervous system. When these are present, when a history of syphilitic infection is obtained and the serological syphilitic reactions are positive the diagnosis is easy; at any rate, the patient should be given intensive antiluetic treatment, remembering, however, that it is possible for a luetic patient to develop a glioma. If the symptoms do not promptly yield, or if they progress under treatment, one should not hesitate to operate, because it has been amply proved that syphilis of the brain, resistant to treatment, often improves promptly after craniotomy (337). The operation should be made under local anesthesia because patients with cerebral syphilis take anesthetics badly (312).

Before the signs of increased intracranial tension appear it may be difficult to differentiate between glioblastoma and arteriosclerosis of the cerebral vessels. The latter can exist when signs of general cardiovascular disease are absent. The symptoms are quite similar in both diseases because they are due to the same cause—thromboses or small hemorrhages within the brain or tumor (363). It may be only when signs of increased intracranial pressure appear that the correct diagnosis is suspected. Of course thromboses of the major cerebral arteries are not apt to be confused because of their characteristic neurological sequels, but repeated smaller softenings lead to difficulty in diagnosis. In the presence of general vascular hypertension another source of error arises. Increased intracranial tension, splitting headaches, and even actual choking of the optic discs may be due to general vascular hypertension alone. A few small softenings are all that are needed to complete the similitude. The fact that a patient with vascular hypertension may develop a tumor is of little practical importance because any attempt to operate for brain-tumor on a patient with vascular hypertension ordinarily ends in disaster from cerebral hemorrhage.

There is no question that various types of encephalitis of known or unknown origin may cause choking of the optic discs and increased intracranial tension (295). Usually in these cases the absence of localizing symptoms makes one suspicious and various concomitant symptoms, such as fever, palatal weakness, or ocular palsies, point to the correct diagnosis.

Glioblastoma developing in the frontal lobes, corpus callosum or left temporal region may cause such profound intellectual deficit that

a primary degenerative disease is suspected. If the Wassermann reaction happens to be positive, general paresis is diagnosed, otherwise senile or presenile dementia. The inexorable march of events usually clears the situation within a brief time. Because of the age at which these tumors develop, the possibility of metastatic tumor must also be kept in mind and a careful search made for a primary lesion, which is often a symptomless carcinoma of the lungs (see p. 358).

The TREATMENT of glioblastoma multiforme is most disappointing. One needs only a brief familiarity with a few specimens obtained at necropsy, such as I have shown you, to realize that there is a desperate need of some method of establishing the pathological diagnosis (see p. 395) without an exploratory operation; it would save much futile labor. It is obvious that any surgical attack must be radical. The surgeon must cut "high, wide, and handsome" and is immediately checked by a realization of the results of such a procedure. Proposals to remove the entire hemisphere have been made; even though successful, the wreck which would result would rarely be worth preserving. Moreover, numerous are the tumors which spread into the opposite hemisphere (339). No general rules can be laid down. When the tumor lies in the occipital or frontal poles, or even in the right temporal pole, a radical excision may be attempted, elsewhere the surgeon will be guided by his knowledge, or by his temerity, and attempt a partial removal or content himself with a decompression. There remains then only roentgen-radiation which is sometimes temporarily effective but apt to cause hemorrhages into the growth and, if pushed too far, to cause degeneration of the brain (479). In the case of no other tumor of the brain is there so much controversy over the proper management, sufficient evidence that no method is effective.

CHAPTER 15

SPONGIOBLASTOMAS

SYNDROME OF THE OPTIC CHIASM PALLIDAL SYNDROME

SYNDROMES OF THE BRAINSTEM

There is yet another type of glioma which is sufficiently characteristic to justify its description apart. It has a tendency to occur along the brainstem from the optic nerves anteriorly to the bulb posteriorly. It was called "neurinoma centrale" by Josephy because of the resemblance of its structure to that of the acoustic neurinomas. Like the latter tumors it is apt to be associated with general neurofibromatosis. We have usually spoken of it as *spongioblastoma unipolare et bipolare* and by others it is called *spongioblastoma polare*. These terms were intended to distinguish it from the *glioblastoma multiforme* which is also by some authors called *spongioblastoma*. The cells of the latter tumor, however, resemble much less closely than do those of the polar *spongioblastomas* the *spongioblasts* of the developing nervous system. It seems best to restrict the term to the tumors we are now about to study. These *spongioblastomas* occur frequently in the optic nerves, chiasm, and tracts. Although they are not the only gliomas to occur in this region they are the characteristic tumors of these structures. We have two such patients to study today.

The first (CASE XXXVI) is a rather stout girl of fourteen years who was always well until four years ago when she began to notice trouble with reading from the blackboard at school. A year later she had pain in the back. *Spina bifida occulta* was found and a brace was fitted. She wore this for a short time and has not since needed it. I first saw her two years ago. At that time she was rather thin. Over the body were numerous brownish patches, the largest 3 cm. in diameter. There were also numerous subcutaneous violet nodules, attached to the skin and feeling like rangles of vessels. There was a nodule in the right cubital fossa, hard, rounded, about 2 cm. in length by 1.5 cm. in width, not attached to the skin and seemingly in the course of the median nerve. Smaller nodules were palpable along the right supraorbital and left greater auricular nerves. Over the anterior aspect of the right ankle

was a mushy swelling which sagged somewhat and in which numerous hard lumps could be felt. Roentgenogram of the sella turcica showed that the anterior clinoid processes were eroded. The optic foramina were both enlarged, the left much more so (Fig. 122). There was a bilateral optic atrophy, but the upper inner quadrant of the left eye was quite pink. The vision was 0.1 in the right eye and 0.5 in the left eye. The visual fields were greatly constricted, with a remaining island of vision on the nasal side in each eye. A diagnosis of glioma of the optic chiasm was made and roentgen-radiation advised. She was taken elsewhere for advice, where a right osteoplastic flap was turned down and the diagnosis of tumor of the optic chiasm verified but no

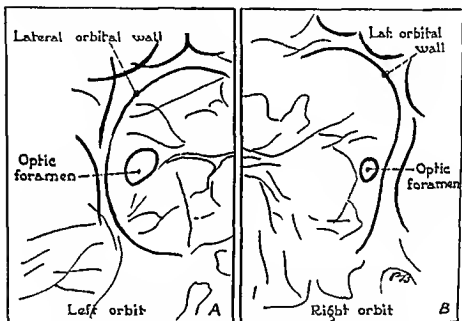


FIG. 122. Schemes from roentgenograms of CASE XXXVI
Compare Plate VII.

tissue was removed for microscopical study. The nodule in the right cubital fossa was also exposed, found to be a fusiform enlargement of the median nerve, and no attempt was made to remove it.

She returned here afterward for roentgen-radiation. She has gained thirty-eight pounds in weight (Fig. 123) and her vision is about the same—right 0.1 and left 0.6. The visual fields are slightly enlarged; there is now a practically complete temporal hemianopia in the left

eye with sparing of macula. In the right eye there is also a temporal hemianopia with sparing of the macula, and in addition a large island of temporal peripheral vision (Fig. 124). Her basal metabolism is now

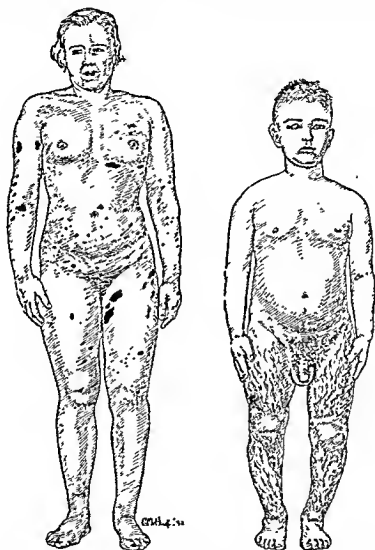


FIG. 123. At the left, CASE XXXVI. Note the pigmented patches and the soft plexiform neuroma above the right ankle. At the right a seven year old boy with pubertas praecox from tumor of the infundibulum.

—11. She has not begun to menstruate. She goes to school and considers herself perfectly well.

The association of these chiasmal gliomas with generalized neurofibromatosis is not uncommon and has long been known. The tumor may be confined to the optic chiasm, tracts, and nerves, but from its

situation one should not be surprised to find the tumor invading or compressing the hypothalamus. We are familiar with the symptoms which one might expect to occur from such an involvement, but in this patient we note only the rather rapid gain in weight to indicate an extension of the growth.

The second patient (CASE XXXVII) has a whole series of symptoms which we have learned to refer to the hypothalamic region. He is a boy of ten years who enters in a wheel-chair because he has just been

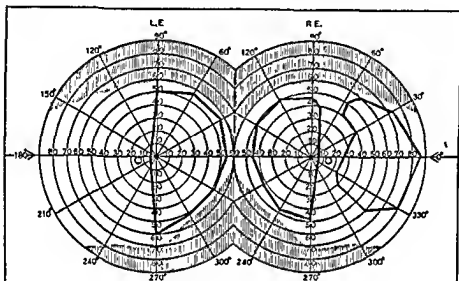


FIG 124 Visual fields from CASE XXXVI.

operated upon. He dates his illness back some four years when his parents noted that he squinted and did not see well with the left eye. In his previous history we find of interest only that he weighed twelve pounds at birth and was always big for his age. When started to school at the age of five he was as big as his brother of seven. He always did his school-work well. He complained of occasional headache since the age of five years and there was a period about that time when he drank excessively and wet the bed at night. The thirst later disappeared but the bed-wetting continued. A year ago he had severe headaches with vomiting. After this he lost ambition, slept much during the day, and gained twenty-five pounds in weight. His memory failed so that he could no longer keep up his school-work.

When admitted to the hospital a couple of weeks ago he was very indifferent, but oriented. He slept a great deal and was content to lie in bed, never asking to get up and never asking about his parents. He was occasionally incontinent. He was obese (weight, 55 kilograms; height, 157 centimeters). His basal metabolic rate was -30 . His head was enlarged and gave a "cracked-pot" note when percussed. The skin was smooth and delicate, the body hairless. The genitalia were small; the testes were descended but very small. The pupils were dilated. The right reacted consensually but not directly, the left reacted directly but not consensually; convergence was impossible. There was a complete primary right optic atrophy. The left optic disc was pale in its temporal half but the nasal half was pink; the margins of this disc were blurred but no elevation was measured. There were no changes in the retinal vessels, no hemorrhages or exudates. He could count fingers with the left eye but it was impossible to plot the visual field because he did not cooperate. Roentgenogram of the head disclosed a dilatation of the sutures and enlargement of the sella turcica with marked erosion of the anterior and posterior clinoid processes. No calcification was seen in the suprasellar region. There was no polyuria and no polydipsia.

The condition was thought to be due to a suprasellar cyst, although there was no suprasellar calcification, and an attempt was made to puncture it through a dilated suture of the skull without success. Roentgenograms were then made of the optic foramina. The left was only slightly dilated but the right could not be certainly identified. It seemed either not to show in the roentgenogram or to be so dilated as to be unrecognizable. The diagnosis remaining in doubt, a right frontotemporal osteoplastic exploration was made under local anesthesia. The lateral ventricle was punctured, the dura mater opened and the frontal lobe retracted. In place of the right optic nerve could be seen a grayish mass of tumor with a large tortuous vein on its surface. It contained a cyst from which 4 ccm. of yellow clotting fluid were obtained. The anterior wall of the cyst was removed. The wound was then closed. The child was not much affected by the operation except that his temperature rose to 39.4° and has not entirely subsided to normal now on the fourth postoperative day. His water-intake has increased only slightly. The tumor was shown to be a spongioblastoma by microscopical examination.

In this case the adiposity, polyuria, somnolence, and genital atrophy all indicate that the hypothalamus has been badly damaged by the tu-

mor. These two patients illustrate practically all the salient features of GLIOMAS OF THE OPTIC CHIASM, as they are called, although they rarely are confined to the chiasm alone but may involve the optic nerves even as far as the retina, also the optic tracts and, as we have learned, even the hypothalamus as well.

These tumors usually cause symptoms in childhood (338), rarely later than young adult age. They are often associated with generalized neurofibromatosis. Hypothalamic symptoms are the rule, adiposity being the most common, but polyuria, somnolence, and genital atrophy also occur. The most significant signs are ophthalmological. The visual fields are usually generally constricted, with bizarre outlieos, although a homonymous or bitemporal defect is not uncommon. Rarely is there a clean-cut hemianopia. The appearance of the fundi is often confusing. The appearance may be that of a primary optic atrophy, or a frank papilledema, but usually there is a mixture of atrophy and swelling. Sometimes there is not enough visible change to account for the loss of vision, or the atrophy may be too great to be accounted for by the degree of choking of the discs. Bizarre combinations of visual findings in a child should always arouse suspicion. It is strange that the appearance of a retrobulbar neuritis with central scotoma is rarely produced. The sella turcica is often eroded, especially around the anterior clinoidal processes. The reason is readily understood when the optic foramina are visualized since they are often widely dilated by the tumor extending through them; usually one is much more affected than the other. Rarely the intra-orbital part of the tumor is sufficiently large to cause exophthalmos.

Gliomas of the optic chiasm must be diagnosed from other tumors in the neighborhood of the chiasm, chiefly hypophysial adenomas and craniopharyngiomas. The adenoma is usually readily excluded; the ballooned sella is lacking and the patient is too young. The craniopharyngioma is not readily excluded if its telltale suprasellar calcification is absent. In this case one can be certain only by demonstrating the dilatation of one or both optic foramina which never in my experience is produced by the craniopharyngioma. The examination of a child with hypothalamic symptoms should never be considered complete without roentgenograms of the optic foramina. There is also a rare meningeal tumor which develops in the sheaths of the optic nerves. Its symptoms may be identical with those of gliomas of these structures but it usually occurs in adults.

The treatment of gliomas of the optic chiasm is naturally rather unsatisfactory. It is not advisable to extirpate them because of the inevitable resulting blindness. Moreover, the mere exposure at operation of one of these tumors is often followed by hyperthermia and death. The attempt to remove the tumor would merely increase the injury to the already involved hypothalamus and the operative mortality would

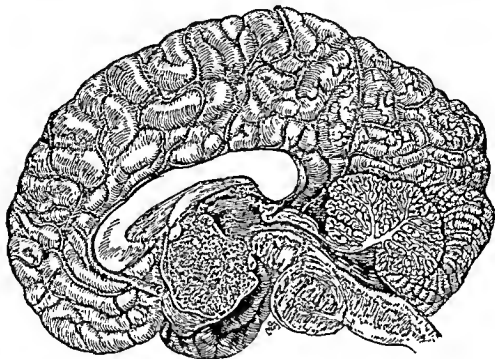


FIG. 125. Median section of a brain with a spongioblastoma of the optic chiasm.

be great. Luckily these tumors are fairly benign; roentgen-radiation arrests their progress rather effectively and even brings improvement in vision. The preoperative diagnosis is, therefore, important because it is the only glioma, with the exception of pontine gliomas, that it is advisable to radiate before operation. Even a subtemporal decompression may cause death from hyperthermia.

When exposed at operation one sees a reddish-gray swelling of the chiasm, or of one or both optic nerves anterior to the chiasm. Sometimes the swelling of one nerve is so great as to obscure entirely the chiasm and opposite nerve. At necropsy the extent of the tumor is sometimes surprising. It may occupy the anterior half of the region of the third ventricle, flattening the hypophysis into the sella (Fig.

125). The tumor may extend up to and obstruct the foramen inter-ventriculare and often extends outward along the optic nerves even as far as the retinae. The tumor is constricted at the optic foramina and

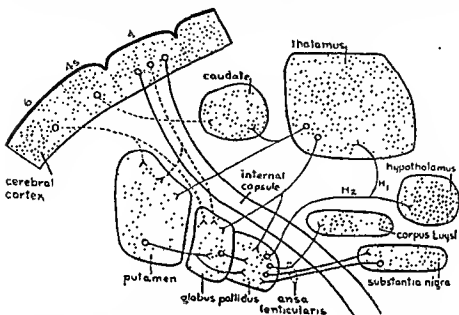


FIG. 126. Scheme of the basal ganglia and their connections (after Kennard).

ophthalmologists operating on the intra-orbital portion often have not appreciated the intracranial extent of the growth until a hyperthermia developed and the patient died from an apparently simple intra-orbital operation. The tumors of the chiasm are usually spongioblastomas, (235) and gliomas of similar structure may arise anywhere in the brain-stem or basal ganglia.

I have already discussed the symptomatology which may result from lesions of the basal regions of the brain which involve the hypothalamus (p. 132) and the thalamus (p. 269). I should here mention briefly another group of nuclei and their associated pathways which are known as the **BASAL GANGLIA**. They may be divided into two parts—the *striatum*, composed of the caudate nucleus and putamen and the *pallidum*, composed of the two segments of the globus pallidus. The caudate nucleus and putamen have the same microscopical structure and are only artificially separated by projection-fibers; they are really one nucleus. The structure of the pallidum is quite different. The amygdaloid nucleus and claustrum, often considered to belong to the group of "basal ganglia," are of less importance clinically.

The striatum receives a projection from various areas of the cerebral cortex (177) and sends fibers to the pallidum, perhaps also to the substantia nigra. The pallidum receives fibers from the striatum, from the subthalamic nucleus and perhaps from restricted areas of the cerebral cortex. It sends fibers to the subthalamic nucleus, to the hypothalamus and, via the ansa and fasciculus lenticularis, then the fasciculus thalamicus, to the nucleus ventralis anterior of the thalamus (400). The connections of the substantia nigra are not finally established. It is doubtless closely related to the pallidum, having a similar chemical composition, and sends fibers to it. These ganglia have a great influence on skeletal muscular activity but the manner of their action is only beginning to be understood (86).

Very marked degenerative changes occur in the striatum in cases of a disease (Wilson's) known as progressive lenticular denegeratioo, also in cases of pseudosclerosis (Westphal-Strümpell), in cases of progressive lenticular dystonia, of double congenital athetosis and of poisoning with carbon monoxide. These affections are all roarked by irregular muscular movements—tremors, chorea, athetosis, dystonias, spasms. But, since in these diseases the lesions are not confined to the striatum and since tremors and other irregular muscular movements may result from lesions of other regions, such as the nucleus subthalamicum or superior cerebellar peduncle, it seems impossible at the preseot time to enumerate the symptoms characteristic of a striatal syndrome. Movements of these types are rarely seen with brain-tumors and are of doubtful significance for localization (362). Another symptom often observed in the above-mentioned diseases is muscular hypertonicity, but this symptom reaches its acme in paralysis agitans (Parkinson's disease) especially in the so-called Parkinsonian states following epidemic encephalitis. Since in these cases the degenerative changes seem to predominate in the pallidum, and the closely related substantia nigra, these states ate often spoken of as constituting the pallidal syndrome (514). I have here a patient with a very pronounced pallidal syndrome.

He (CASE XXXVIII) is a man sixty-six years of age, who was sent to this clinic suspected of having a tumor of the brain. He had always been well and active in his business until six years ago when he had an attack of vomiting and was advised to enter a hospital. Here his sinuses were examined because of his complaint of headache, but nothing abnormal was found. He was treated for duodenal ulcer although no positive evidence of an ulcer was obtained. About a year later he had another attack of vomiting with headache and at this time it was

noticed that his right leg was weak. Occasional attacks of vomiting recurred during the succeeding years until two years ago when a particularly severe attack of headache and vomiting sent him again to the hospital for a few days. Although he was not unconscious at the time he had subsequently no recollection of having been in the hospital. Six months later his friends noted that he handled himself clumsily, especially in going up or down stairs, and that he spilled his food often. Another attack of headache and vomiting during which he was drowsy and tired was followed by increasing difficulty in walking. He tried osteopathic treatments but they seemed to increase his headache and he continued to vomit. He finally became bedridden, his memory failed and he seemed to "think less well."

The patient lies in bed motionless and one is immediately impressed by the expressionless face. It is as if frozen. He does not answer questions but continues to stare directly ahead. After a moment one observes what is peculiar about this stare—the fact that he never winks. The expression in his eyes is clearly unfriendly. Previously he was somewhat amused by our examinations but has lately become irritated by what he calls our "monkey business." He coöperates very little during the examination. He can open and close his hands slowly but when urged to put his finger on his nose he moves the arm very little and only after a long delay. In the right hand is a very definite forced grasping.

When an attempt is made to move the limbs passively we find to our surprise that they are very stiff. It requires considerable force to bend the joints. It is equally difficult to extend them. The impression which one gets is entirely different from that we have already studied in pyramidal lesions. In this case the muscular rigidity involves all the muscles of the limbs, although the hands and feet are less rigid than the proximal segments. It should be noted also that the limbs remain in the position given them; they can be moulded like a "lead pipe." There is no tremor of the limbs but the movement of the elbows gives a "cog wheel" impression to the examiner's hand, especially on the right side. The rigidity extends even to the trunk. When asked to get out of bed he has to be assisted to sit up. He comes up all in a piece like a tin-soldier; there is an absolute lack of the usual automatic syncinetic movements. When placed on his feet he walks with short stiff steps and with a total absence of the usual automatic movements of walking. He has to be supported, else he falls over backward.

The tendon-reflexes are all present but seem not to be exaggerated. The plantar reflex on the right side is not definitely normal. I persist

rather too long in my testing and suddenly he ejaculates "Gad! isn't that enough?" and again "What the hell is the use of all this?" It is sufficiently evident that he can speak and he also comprehends well but it takes him a long time to respond. The right optic disc is normal; the left is blurred and slightly elevated. It is impossible to examine the visual fields. The left pupil is twice as large as the right but both react promptly to light. No sensory defect has been detected although examination is not satisfactory. Roentgenogram of the head showed the dorsum sellae to be decalcified as from long-continued intracranial tension.

It would be difficult to find a more complete PALLIDAL SYNDROME. I have never seen such a pronounced rigidity associated with a tumor of the brain, yet the history is very suggestive of tumor and such instances have been described (368). His spinal fluid has been found normal. There is no evidence of lues or arteriosclerosis. The history is not at all that of encephalitis or multiple softenings, or of the ordinary paralysis agitans. It was determined to make an encephalogram to help clear the diagnosis. An encephalogram was chosen rather than a ventriculogram because I wanted to visualize especially the basilar regions of the brain. The encephalogram reveals a marked bilateral hydrocephalus. The septum pellucidum is displaced slightly to the left. The third ventricle seems to be pushed upward and forward. The aqueduct (of Sylvius) seems also to be displaced upward and backward and the distance between it and the basilar cistern seems abnormally great. There is no air in the fourth ventricle. The encephalogram seems to indicate an expansive lesion in the tegmentum mesencephali, perhaps extending forward into the basal ganglia, but we cannot put too much faith in our interpretation of these complicated shadows. At any rate, *if a neoplasm is actually the cause of this man's difficulties, it is in a situation which precludes any attempt to deal with it surgically.* The absence of choking of the optic discs does not argue against the possibility of a glioma in this situation. It is a strange fact that the *gliomas of the brainstem cause swelling of the optic discs very late.* Gliomas in this situation are often spongioblastomas. Since they are essentially benign tumors this possibility explains well the length of his clinical history.

When these tumors lie still farther down the brainstem other clinical pictures are produced. The term BRAINSTEM means technically all the segmental apparatus of the brain, but I use it here in the more restricted sense of the constricted portion of the brain extending from the mammil-

lary bodies and subthalamus to the point of exit of the first cervical nerve. Since nearly all of the cranial nerves enter or leave this portion of the neuraxis and since it is traversed by all the long projection-pathways from the cerebrum to the spinal cord it may be understood that *the symptomatology of its tumors is dominated by palsies of the cranial nerves and by various manifestations of quadriplegia*. I will mention a few of the combinations which may result as they are described in the classical

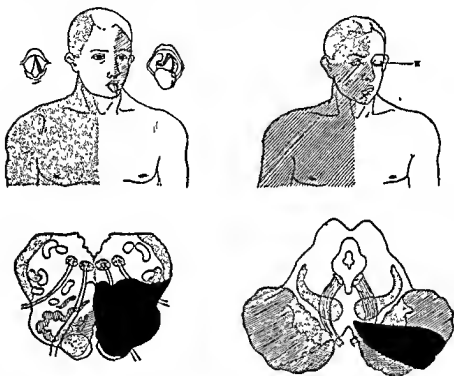


FIG. 127. At the left, thrombosis of the left vertebral artery causing right hemiparesis and hemianesthesia (except face), and on the left side a syndrome of Avellis associated with lingual hemiatrophy, hemicerebellar syndrome, oculopupillary troubles, and facial anesthesia. At the right, hemorrhage into the left cerebral peduncle causing paralysis of the left oculomotor nerve and a right hemiplegia (after Dejerine).

syndromes (Fig. 127). In the medullary syndrome (of Avellis) one finds paralysis of the soft palate and vocal cord, accompanied often by hemianesthesia and hemiparesis of the opposite side and by other symptoms. In the anterior pontine syndrome (of Millard-Gubler) there is a contralateral hemiplegia without involvement of the face, and on the

side of the lesion an internal strabismus from palsy of the sixth nerve and a complete facial palsy. In the pootioe syndrome (of Foville) the contralateral hemiplegia includes the lower face; there is also a contralateral hemianesthesia, and on the same side palsy of the sixth and seventh nerves and of conjugate lateral movements of the eyes to the side of the lesion, the patient looking toward the paralyzed side and away from the lesion. In the anterior peduncular syndrome (of Weber) there is contralateral hemiparesis including lower face and tongue, with (on the same side) paralysis of the third nerve causing ptosis, divergent strabismus and mydriasis. In the posterior peduncular syndrome (of Beodict) there is a crossed hemianesthesia and choreo-athetoid movements associated with the homolateral palsy of the third nerve. These examples will suffice to illustrate the kind of alternate palsies which are produced by lesions of the brainstem. The combinations just cited are caused by vascular lesions and recur with some frequency since each is due to softening of a certain vascular area. They are marked by sudden onset often with coma. But *when similar alternating palsies develop slowly and progressively, especially in young persons and before symptoms of intracranial hypertension occur, the presence of a tumor of the brainstem may be suspected.* I can show you some fairly typical examples.

Here is a small patient (CASE XXXIX) who possibly has such a tumor. She is four years old and has always been well except for a mild scarlet fever at the age of two years. Two months ago her mother noted that the right eyelid drooped. A month later the left side of the mouth drooped and the left arm was used awkwardly. Soon afterward the left leg became weak. Three weeks ago she vomited for the first time. For the last three weeks she has been unable to walk. For the last two weeks her respirations have been irregular with many deep sighs. A week ago she had a headache for the first time, her breathing became seriously impaired and she was brought to the hospital.

When admitted she lay in a semi-comatose state with the head turned to the left side and could be aroused to answer questions only in monosyllables. The left arm was spastic and semiflexed; the left leg was rigidly extended. There were continuous athetoid movements of the right arm and leg. Respirations were slow, deep, and sighing. The right pupil measured 4 mm. and was fixed to light. The left pupil was 2 mm. in diameter and reacted sluggishly. The optic discs were normal. There was a ptosis of the right eyelid. The right eye was turned down and out. There was a slight left facial weakness of peripheral

type on emotional stimulation. Hearing was definitely impaired, more on the right side. Swallowing was normal. The tongue protruded in the midline. Tendon-reflexes were brisk on both sides but more on the left. There was a clonus at the left ankle. There was an extensor plantar reflex on both sides, much more easily elicited on the left. Roentgenograms of the head were normal; the sella turcica was not eroded. There were periods of easy quiet respiration. But occasionally deep sighing respirations were interspersed and with each one the head was retracted and turned to the left and the right shoulder was lifted off the bed as the body was rotated to the left; at the same time the spasticity of the left side increased and the right side became quiet. Today you see that both arms and legs are rigid. She does not move any extremity voluntarily but from time to time there are clonic spasms of the right arm and leg. Her head is in the midline and not retracted. There is a clonus at each ankle and an extensor plantar reflex on each side. She does not respond to questions. There is still no edema of the optic discs. The symptoms resembled in the beginning those of the posterior peduncular syndrome (of Benedict) and the tumor doubtless lies mainly in the right cerebral peduncle. No operation has therefore been undertaken.

This male child (CASE XL), five years of age, had been well except for an uncomplicated mumps until about six months before his admission to the hospital. At that time he seemed languid and not disposed to play. He whined and complained a great deal and twice vomited. But nothing very abnormal was noticed until seven weeks ago when he began to vomit persistently. He vomited at any time, suddenly and violently without nausea. Shortly afterward began a nodding tremor of the head and difficulty in walking. He staggered as if drunken and also dragged the left leg. His speech became nasal and indistinct. He complained very little of headache.

When admitted to the hospital he lay listlessly in bed. There was no "cracked-pot" sound when the head was percussed and the neck was neither stiff nor tender. The optic discs were not choked. There was no obvious squint but the child seemed to be unable to move the eyes conjugately to either side. There was a paresis of the left facial nerve of peripheral type. The tongue protruded to the right; there were twitchings of the whole organ. The palate lagged on the left side. His speech was dysarthric and nasal. There was a left spastic hemiparesis with clonus of the ankle and extensor plantar reflex. There was no

clonus on the right side and no spasticity but an extensor plantar reflex was obtained also on this side. It was impossible because of lack of coöperation to examine satisfactorily smell, hearing, and general sensibility. The right corneal reflex seemed diminished and the abdominal and cremasteric reflexes were not obtained.

With obvious difficulty of conjugate lateral movements of the eyes, paresis of the left seventh and tenth nerves, possibly also of the right fifth nerve, evidence of involvement of both pyramidal tracts and no symptoms of increase of intracranial tension a tumor of the brainstem in the region of the pons and bulb seemed most probable. The outlook seemed hopeless but on the chance that a cystic tumor might be present a suboccipital exploration was made. Under local anesthesia the suboccipital region was opened through a midline incision. The tonsils were not herniated into the foramen magnum. When the tonsils were separated the bulb could be seen to be greatly increased in size in every diameter. The floor of the fourth ventricle was bulged dorsally. No evidence of a cystic cavity was found by palpation so the wound was closed. The child's temperature went up to 40°; otherwise he was not much upset by the exploration. It is now two weeks later. He lies in a semi-stuporous condition staring straight forward. He makes constant sucking movements with his mouth and tongue. He reacts to a loud noise by a start and a turning of his eyes downward and inward in a convergent spasm. He can move his eyes upward but apparently not laterally. The pupils react to light; the right corneal reflex is absent. He cannot swallow. The left arm and both legs are spastic. The right arm is flaccid. The abdominal reflexes are not obtained. The absence of the right cremasteric reflex can be explained by the fact that the right testis has not descended into the scrotum; the left is present.

The diagnosis of tumors of the brainstem is often difficult because of the absence of signs of increased intracranial tension (36). The acute forms of polioencephalitis, whether the superior type of Wernicke, the inferior type of Leyden or the mixed types associated with infectious diseases are relatively easily differentiated. But the chronic forms may cause difficulty. When the lesions remain confined to the motor nuclei in typical cases of progressive nuclear ophthalmoplegia or Duchenne's progressive bulbar palsy confusion will not arise because tumors of the brainstem are almost always associated with signs of involvement of the pyramidal tracts and sensory pathways. But a bulbar palsy may be only a

part of an amyotrophic lateral sclerosis, of a multiple sclerosis, of bulbar lues or other infectious or degenerative diseases. The diagnosis is then often impossible in the early stages and becomes clear only after the development of other more characteristic signs of the causative disease. It is to be noted, however, that these chronic degenerative and infectious diseases of the brainstem are found almost exclusively in adults. In childhood progressive palsies of the lower cranial nerves have in my experience always been found ultimately to be due to tumor. Formerly tubercle was common and practically impossible to differentiate, but is nowadays very rare.

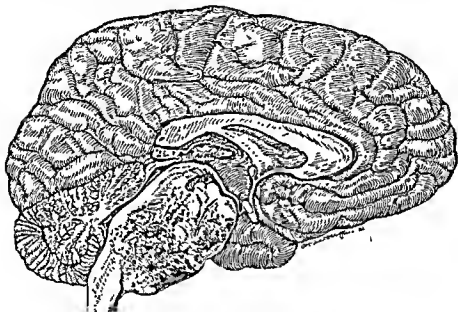


FIG. 128. Median section of brain with spongioblastoma of the pons.

In children tumors of the brainstem must be differentiated mainly from cerebellar tumors. The diagnosis is usually not difficult. Tumors of the brainstem cause intracranial hypertension late and persistent vomiting, stiffness of the neck and unsteady gait may precede its onset by a considerable period. Cerebellar tumors do not cause palsies of the cranial nerves until late and then usually only weakness and not the complete paralysis seen with tumor of the brainstem itself. Of course if the patient is seen late in the course of his illness and a good chronological history cannot be obtained the differentiation may be very difficult. It should not be forgotten also that a tumor may involve both the

cerebellum and brainstem.

In adults confusion is apt to arise with acoustic neurinoma if the tumor lies mainly in the pontine region. But the acoustic tumor by the time it involves other cranial nerves than the eighth has usually caused obstruction of the circulation of cerebrospinal fluid and symptoms of intracranial hypertension. If one keeps in mind the regular march of events in acoustic tumors fewer errors will be made. In pontine tumors the auditory symptoms are apt to occur late, the

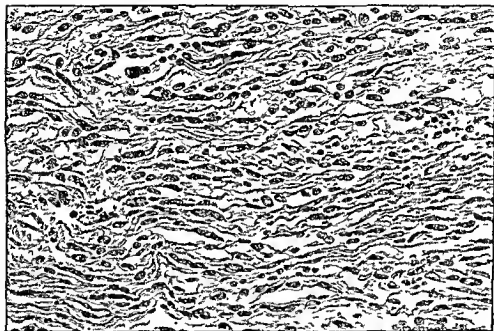


Fig. 129. Drawing of a microscopical preparation of a spongioblastoma.

patients do not complain of suboccipital discomfort, vertical nystagmus is frequent, and symptoms of intracranial tension may be absent long after there are marked cerebellar disturbances and extensive palsies of the cranial nerves.

From tumors of the pineal body (cf. p. 347) tumors of the brainstem differ in many ways. In pineal tumors paralysis of the conjugate upward movement of the eyes occurs; with pontine tumors paralysis of the conjugate lateral movements. Palsies of the cranial nerves occur late with pineal tumors whereas they are early with tumors of the brainstem. Pineal tumors cause intracranial hypertension early, perhaps by obstruction of the great cerebral vein (of Galen) as much

as by obstruction of the circulation of cerebrospinal fluid. The symptoms of pineal tumors have a tendency to be bilaterally symmetrical, especially the deafness.

While all tumors of the brainstem are not SPONGIOBLASTOMAS, this particular type of glioma is frequent in this region (384) just as it is in the optic chiasm. The spongioblastomas are relatively benign tumors which usually show little evidence of active growth. Their average time of evolution, forty-nine months, is undoubtedly shortened by the frequently unfavorable situation of the tumors. They may give symptoms at any age but are especially liable to cause symptoms in childhood when they occur in the optic chiasm. In this situation they are also frequently associated with peripheral manifestations of neurofibromatosis. In the pons they cause a great swelling which was formerly described as hypertrophy of the pons (Fig. 128). In gross appearance the spongioblastomas are reddish gray, relatively avascular and soft. They are not encapsulated but are usually fairly sharply circumscribed. Cystic degeneration is frequent but fatty degeneration and hemorrhage are rare.

The MICROSCOPICAL STRUCTURE is composed mainly of bipolar and unipolar cells which resemble somewhat the spongioblasts of the developing brain. The exact nature of the neoplastic cells is disputed. They have been thought to be elongated astrocytes or even oligodendroglia. They have oval nuclei with abundant chromatin. Mitoses are rare. Each cell has one of more long processes which stretch for long distances in the tissue and, since they have a tendency to lie parallel to each other, give a characteristic appearance to the tissue (Fig. 129). There are rarely differentiated neuroglial fibrillae; usually the processes are stained as a whole by methods for neuroglia. The processes do not have any connection with the rare bloodvessels which traverse the tumor. They often undergo a sort of hyaline transformation, after which they stain very heavily and are sometimes swollen and beaded or twisted spirally (50). Occasionally calcium-salts are deposited in these hyalinized masses.

The prognosis of the spongioblastoma would be good if it were not for its often unfavorable situation which makes removal by operation impossible. TREATMENT is, therefore, often restricted to roentgen-radiation which sometimes improves even those involving the optic chiasm. Occasionally a cystic spongioblastoma of the cerebellum is encountered which can be removed and in these cases the patient remains permanently well.

CHAPTER 16

PINEALOMAS

SYNDROME OF THE PINEAL REGION

DECEREBRATE SYNDROME

Tumors of the pineal body are interesting, among other reasons, because the occasional associated symptoms of *pubertas praecox* gave rise to the hypothesis that the pineal body was a gland of internal secretion. The association of this developmental anomaly with increased intracranial pressure is very suggestive of pineal tumor as Frankl-Hochwart pointed out in 1909. Aside from the syndrome of precocious puberty, which naturally can arise only when the tumor develops before the age of puberty, the other symptoms even in adults are sufficiently characteristic to enable one to make a diagnosis of pineal tumor with considerable certainty in many cases.

This woman (CASE XLI) of thirty-two years is suffering from a pineal tumor. She says that she was always well and in good health until ten months ago when she ceased menstruating and began to have intermittent headaches. The patient dates her illness from this time, but her sister informs us that as early as three years ago she began to be careless of her home and person, whereas previously she had been neat and a good housekeeper. She seems to have been also increasingly irritable. At any rate since ten months ago she was definitely ill with headaches which were at first in the temples and later frontal. At first two or three days would pass without headaches, but in the last five months they became constant and her vision failed. She consulted various doctors, who, because of the cessation of her menses, diagnosed endocrine disturbances and gave her ovarian and thyroid extracts. She had glasses fitted by an optometrist; they did not help her vision. About this time her sister noted that she spilled her food and that she often seemed not to hear what was said to her. She began to walk with her chin held high. Her gait became unsteady and she often fell backward. Two months ago a physician made a lumbar puncture, after which she was much worse. She went about as in a dream; her vision and hearing rapidly failed. She grew quite stout.

When admitted to the hospital she was very lethargic. There were bilateral choked discs of 2-3 diopters elevation with scars and second-

ary atrophy. The visual acuity of the right eye was 0.2 and of the left eye 0.2—1; the visual fields were generally constricted. The patient was unable to converge the eyes and was unable to look above the horizontal plane. There was a palsy of the left sixth nerve. The pupils reacted feebly in accommodation and not at all to light. They were moderately dilated and equal in size. Hearing was greatly diminished on both sides, both to conduction by air and by bone. There was a coarse tremor of the right hand. The gait was very unsteady, with a tendency to fall backward. The tendon-reflexes were all very brisk but no clonus was elicited. There was an extensor plantar reflex on both sides. Both legs were weak, especially the flexor groups of muscles. No asynergia or dysmetria of the extremities was found. The pelvic examination was normal. The basal metabolic rate was —20. The roentgenogram of the head showed that the posterior clinoid processes were absent. No calcification was seen in the region of the pineal body. The clinical impression was tumor of the pineal body.

A right subtemporal decompression was made as a preliminary to roentgen radiation. The roentgen treatments have now been completed in a series of small doses. The decompressed area is bulging and fairly tense. She has very little headache and is much more alert. The optic discs are still choked to 1.5 diopters. She is still quite deaf. You see that she cannot turn the eyes upward or downward and that the left eye does not turn beyond the midline when she tries to look to the left.

The characteristic symptom in this case is the inability to look upward. Paralysis of conjugate movement of the eyes upward occurs mainly by involvement of the tectum mesencephali and, since tumors of the tectum are excessively rare, practically only by pressure from above. The tumors which develop in the supratentorial region are almost exclusively of pineal origin (230). This symptom combined with intracranial hypertension is, therefore, almost certainly diagnostic of pineal tumor. One should be careful, however, in interpreting this symptom in children, who seem to have difficulty in looking upward when they have an internal hydrocephalus from any cause.

Because of its situation the tumor causes other symptoms from involvement of nervous structures. Often the pupils are fixed and do not react to light although they may contract promptly in convergence and accommodation. (513). Bilateral partial deafness is often caused by pressure downward on the medial geniculate bodies which are,

of course, a relay-station for the conduction of impulses from the cochlea to the cerebral cortex. By pressure on the superior cerebellar peduncles marked cerebellar disturbances are produced and pineal tumors for this reason are often operated on with a mistaken diagnosis of cerebellar tumor. Nystagmus is not frequent. Bilateral spasticity of the lower extremities may occur; on the other hand numbness and objective sensory loss are rare (274) and pareses of the cranial nerves, aside from the conjugate difficulty just mentioned, are rare. The symptoms and signs of intracranial hypertension occur early.

In most discussions of the symptomatology of pineal tumors much is made of a constitutional disturbance known as MACROGENITOSOMIA PRAECOX. The term means that the child affected develops physically earlier than normally and this precocious development is especially evident in the genital system. The syndrome is rare with pineal tumors, and found practically only in male children. The mechanism of its production is not known. It has been generally believed that the pineal body furnishes a secretion which holds the development of the genitalia, also of the whole body to a certain extent, in check. At puberty an involution of the pineal body is supposed to happen, which diminishes its secretion, thus allowing sexual development to occur. There is little evidence to support this theory. The pineal primordium is known to form in certain lower vertebrates a median eye. In the human being the pineal body is composed largely of a peculiar type of neuroglia with abundant septa of connective tissue. During development there are for a time ependymal canals, which later disappear. There is no evidence at any time of secretory activity and no evidence of any sudden change in structure at the time of puberty. There are many cases of destruction of the body by tumor before puberty without *pubertas praecox* and this syndrome may be produced by tumor elsewhere (275) while the pineal body is apparently normal (cf. Fig. 123). So that *although precocious puberty plus intracranial hypertension usually means a pineal tumor, the localization always needs confirmatory evidence.* I can show you such a syndrome.

This boy (CASE XLII) of twelve years had always been well until six months ago when at the beginning of the school-year he complained that his eyes ached if he tried to read. Bright light was also very painful and he preferred to remain in a darkened room. Two months later he began to have severe pains over the eyes, first in the left frontal region and then on both sides. He complained also

of buzzing and singing in both ears. He vomited a few times when the pain in his head was very severe. His vision began to fail and he was brought to the clinic.

He entered in a lethargic condition. He kept his eyes closed. When he opened them there seemed to be a slight ptosis of the left eyelid. The pupils were dilated, the left more so. Both reacted very slightly to bright light. He could apparently not converge his eyes. Conjugate upward movements were very limited and poorly sustained. There was a weakness of the left external rectus muscle. The optic discs were swollen about 3.5 diopters. Visual acuity was 0.4 with the right eye and 0.3—1 with the left; the visual fields were normal. Auditory acuity was only slightly impaired for high-pitched tones. There was no weakness of the extremities and no sensory loss. The knee-jerks were weak, the other reflexes normal. There were no signs of involvement of the cerebellum, and the neck was not tender or stiff. The pineal body was seen in the roentgenogram to be calcified and displaced downward and to the right of its normal position.

Most important, however, was the general bodily appearance of the boy (cf. Fig. 123). He was 149 cm. in height and weighed 37.5 kg. He had a deep masculine voice. His body was covered with a fine silky hair and he had considerable hair over the face and upper lip. The external genitalia were of adult size and there was an abundance of black pubic hair. His father told me that his voice began to change and that the growth of hair and external genitalia occurred also about the same time as the onset of visual troubles.

A diagnosis of pineal tumor was made. It was planned to give him roentgen treatments. As a preliminary the ventricles were punctured so as to have a means of quick relief if he should react badly to the treatments. After the puncture, which was made with local anesthesia, he became semiconscious and exceedingly restless. He tossed and wriggled constantly. His face was very flushed although he had no fever. His pulse rate varied rapidly from 100 to less than 60 and he had periods of rapid deep respirations. There was a spontaneous nystagmus with the quick component to the right. After two days these symptoms disappeared. He was given a third of an erythema dose of roentgen-radiation. A few hours later he was comatose, the ventricle had to be punctured and a right subtemporal decompression made. After that procedure he improved somewhat but it was necessary to puncture his ventricles repeatedly. It was obvious that

the obstruction to the aqueduct was complete and that an immediate attempt to remove the tumor was unavoidable.

Under anesthesia with ether a boneflap was turned down in the right parietal region. The bone was rongeuired away up to the sagittal sinus, the dura mater opened and the cerebrum retracted, after ligation and division of one posterior superior cerebral vein. The greatly thinned splenium of the corpus callosum was divided and the grayish mass of the tumor exposed. Large veins could be seen on its surface. The capsule was split and the tumor found to be so tough that it was necessary to use the electric loop to remove it. The portion to the right of the falx cerebri was removed, but the lower border of the falx was firmly adherent to the tumor and an attempt to divide it provoked a profuse hemorrhage which was checked with difficulty. The wound was therefore closed with a drain left in the cavity of the tumor. To my surprise there was no subsequent hyperthermia; the temperature continued to oscillate between 37° and 38° . The boy lay quietly, seeming to be peacefully sleeping. The eyes rolled slowly from side to side with an occasional convergent spasm. The pupils varied greatly in size and did not react to light. He could not be aroused to respond to any questions. He kept his teeth tightly clenched so that it was necessary to feed him by nasal tube. The decompressed area was very tense and I was obliged to puncture the lateral cerebral ventricles twice daily. There was a bilateral ankle-clonus and extensor plantar reflex although the limbs were fairly flaccid. In flexing the head on the chest to test for signs of meningeal irritation it was discovered that both forearms flexed. When the head was replaced on the bed the arms relaxed. Other movements of the head were then tried and it was found that, when the face was turned to the right, the right arm was extended and there was a slight extensor movement of the right leg. At the same time the left forearm was flexed and the left leg did not move. When the face was rotated to the left the left arm extended, the right leg relaxed and the right arm was flexed.

These associated movements convinced me that there was a setious compression of the brainstem for reasons which I will explain in detail a little later. This impression was confirmed by the tension in the ventricles, the absence of hyperthermia, and the unconsciousness. We know in a general way what is meant by the term "consciousness" but no one has ever been able to define it satisfactorily. It would be

foolish to try to locate a function of consciousness in the brain, but a sudden compression of the brainstem at the anterior extremity of the aqueduct will, in my experience, arrest consciousness more effectively than any other lesion of equal magnitude. It was determined, therefore, to make another attempt to remove the remaining tumor. A bone-flap in the left parietal region was made with local anesthesia and the left half of the tumor removed as previously described. The region seemed completely collapsed and was drained as before.

After the last operation his temperature oscillated between 38° and 41° . His general condition remained unchanged. He lay quietly in bed, apparently awake, but made no response to any stimulus. The eyes rolled constantly to the left with an occasional convergent spasm during which the eyeballs were retracted slightly. The pupils no longer oscillated in diameter but remained fixed to light. It is now seven days since the second operation. For the last two days his temperature has remained closely around 39° and he is beginning to moan occasionally. For the first time he objects to nasal feeding. His jaw is relaxed and the tension of his decompressed temporal region is entirely gone. The ventricles can be completely drained by lumbar puncture. He still has a bilateral extensor plantar reflex and the associated reactions persist although not now so marked as formerly. It is these reactions which I want particularly to discuss with you because they are rarely seen in the clinic. You note that when I flex the head on the chest both forearms are flexed and when I replace it on the bed the arms relax. Also when the head is rotated forcibly with the face to the right, the right arm slowly extends and the left is flexed. When the face is rotated to the left, the left arm is extended and the right flexed. The legs do not participate in these movements. These associated movements are rarely seen in patients but are very important because they confirm a long series of brilliant investigations of the physiology of the brainstem of animals. They are illustrations of what has been called the HIERARCHY OF FUNCTIONS IN THE NERVOUS SYSTEM (289).

In the development of the neuraxis one system of neural mechanisms has been superimposed on another, culminating in the cerebral cortex, each superior one modifying the inferior ones. When one of the superior mechanisms is deranged certain symptoms appear which are due to release of the inferior mechanism from control. These symptoms were formerly thought to be due to irritation of the superior

mechanism by the lesion. Although such irritative symptoms occur, and are known in some instances, they are transitory, whereas the phenomena of release are permanent. Many such release-phenomena have been elucidated by the physiologists and a few of them identified in the clinic, but their anatomical correlative mechanisms are imperfectly known. We may outline a few of them briefly.

When the cerebral hemispheres and corpora striata are removed from an animal, say the cat, leaving the thalamus and lower parts of the central nervous system intact, as soon as it recovers from the anesthesia the animal rights itself into its normal sitting position. When placed in any abnormal position it immediately rights itself. Although it remains motionless if left alone, when stimulated it walks, runs, or jumps more or less normally after a few days. Its muscles seem to be perfectly well coördinated. While walking the tone of its muscles is essentially normal. The thalamus may also be removed with no change in motility, but the animals tend to be excessively active and so are not good subjects for experimentation. For the purpose of studying those reflexes which permit these animals to maintain their normal position so-called thalamus-animals are used, that is to say, those in which the thalamus is still attached to the lower portions of the nervous system.

Four groups of *righting reflexes* are isolated in these *animals* (328). If such an animal is held by the pelvis and turned into any position the head is always kept in the normal position in space. The stimulus which makes this possible has been shown to arise in the otolithic apparatus. This reflex is therefore called the labyrinthine righting reflex. When the otoliths are removed the head hangs supinely; but if the animal is now placed in the lateral position on the floor the head is immediately righted into the normal horizontal plane. The stimulus for this reaction arises from pressure of the body on the floor. When a weighted board is placed on the upper lateral surface of the body the head turns back into the lateral position. There is, then, a bodily righting reflex acting on the head. If the animal is lying on the floor and the head has been righted, the neck becomes twisted. This causes stimulation of nerves in the muscles and joints of the neck which in its turn gives rise to a cervical righting reflex acting on the body by which the body is rotated into symmetrical relation to the head. The trunk being then twisted, the pelvis is brought into line. But the animal can right itself even if the head is held in the lateral posi-

tion; as soon as its lateral surface touches the floor it rights itself in spite of the cervical righting reflex which would tend to hold it in the lateral position. More powerful than the cervical righting re-

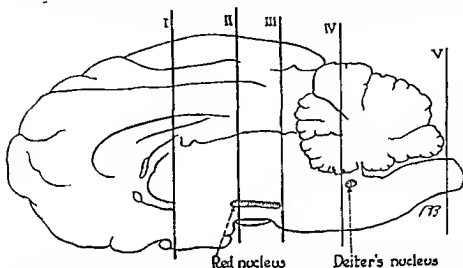


FIG. 130. Median section of cat's brain showing various levels of transection and their effects. I—normal muscular tone, normal temperature; II—usually normal tone, normal righting reflexes, regulation of temperature lost; III—exaggerated muscular tone, labyrinthine righting reflex on the head and the body righting reflex on the body lost (decerebrate rigidity); IV—exaggerated muscular tone, tonic cervical and labyrinthine reflexes persist, righting reflexes lost; V—decerebrate rigidity lost, tonic labyrinthine reflex lost, tonic cervical reflexes on the limbs persist (decapitate animal).

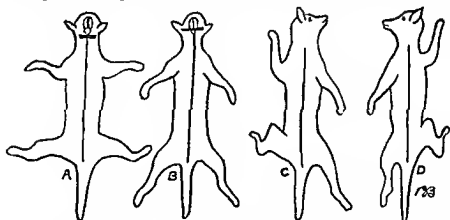


FIG. 131. Series of cats demonstrating effects of various transections of the brainstem. A—decapitate animal; B—decerebrate animal; C, D—effect on the limbs of rotating the head of a decerebrate animal.

flex, therefore, is a bodily righting reflex acting on the body. These are all the righting reflexes in the thalamus-animal. There is, at least in monkeys, also an optical righting reflex which is suppressed by decerebration.

The central mechanism of most of the righting reflexes lies at the level of the red nucleus (329). Their relation to this nucleus is not entirely clear. The cerebellum, however, is not concerned; they persist after its complete removal. By careful decerebration below the red nucleus (Fig. 130, III) the labyrinthine righting reflex on the head and the bodily righting reflex on the body are absent but the cervical righting reflex on the body persists. The neural mechanism for the last reaction is, therefore, situated lower in the brainstem. The bodily righting reflex acting upon the head seems to have its center at the level of, but not in, the red nucleus.

If a transverse section be now made across the cat's brainstem (Fig. 130, III to IV) between the red nucleus and the vestibular nuclei, a most amazing change occurs in the attitude of the animal (Fig. 131 B). Certain muscles become very hypertonic, principally the extensors of the limbs, the elevators of the head, neck, and tail, and the extensors of the spine. The result is that the head is retracted, the tail lifted, the spine and limbs fully extended. The fore legs are retracted somewhat at the shoulder and the footpads are directed ventrally. When such an animal is placed on its feet it stands, but in an exaggeration of the normal standing position. This condition of *decerebrate rigidity*, as it is called, is a part of reflex standing (436). When such an animal is pushed over it cannot regain its normal standing or sitting posture. It lacks entirely the righting reflex characteristic of the thalamic animal. The rigidity in these animals manifests certain characteristics: (1) the muscles oppose any attempt to stretch them but if the passive stretching force is sufficiently strong a reflex inhibition causes the resistance suddenly to collapse; (2) there is a certain plasticity to the rigidity which enables the limb, when placed in any position, to maintain that position for a short time; and (3) the tendon-reflexes are brisk and by timing a succession of jerks the muscle can be progressively shortened.

The condition of decerebrate rigidity depends largely on the integrity of the afferent nerves of the muscles involved but may be modified by changing the position of the head in space or in relation to the body. Strongly flexing the head decreases the tone in the fore

legs and increases it in the hind legs, while elevating the head increases the tone in the fore legs and decreases it in the hind legs. The stimuli for these effects arise in the muscles and joints of the neck. The rigidity is at a minimum when the animal is in normal standing position with the snout at an angle of 45° below the horizontal plane and at a maximum when the animal is on his back with the snout at an angle of 45° above the horizontal plane. The impulses for these latter effects come from the labyrinths and affect all four limbs identically. The rigidity may also be modified by turning the head even if the labyrinths are removed. If it is rotated the tonus of the limbs toward which the snout is turned is increased, whereas the tonus of the limbs toward which the occiput is turned is diminished (Fig. 131, C, D). The impulses for these effects come from the cervical muscles and joints. These effects are due to the changed posture of the neck and persist as long as the new posture is maintained. They are, therefore, called *tonic cervical and labyrinthine reflexes*. The sum total of all the tonic reflexes concerned in reflex standing are called standing reflexes. There are also tonic reflexes of the limbs, on the limbs, which we need not consider in detail. Such is the crossed extensor reflex. If one hind limb of the decerebrate animal be strongly flexed the opposite hind limb is tonically extended. Another example is the extension of the fore limb of the opposite side which may be obtained in favorable decerebrate animals by sudden forceful flexion of the knee-joint against the resistance offered by the quadriceps femoris muscle (385). The details of the standing reflexes vary in different species of animals. For example in the sloth, which hangs by its feet from the limbs of trees, the rigidity affects the flexor muscles (403). It seems, therefore, that the condition involves principally the antigravity muscles. In the cat the rigidity affects also the elevators of the lower jaw which, of course, have nothing to do with standing.

The exact tracts and nuclei involved in decerebrate rigidity are not definitely known. If successive transverse sections of the brainstem are made the condition appears when the section reaches the posterior border of the anterior colliculus above and the posterior border of the mammillary bodies below. It persists after removal of both labyrinths and the cerebellum. (The cerebellar vermis is, however, able to cause a diminution of the rigidity as we have seen). It is not abolished by section of the posterior columns of the spinal cord but disappears by section of the brainstem only when the cut passes back

of the vestibular nuclei. The efferent pathway seems to be the vestibulospinal tract (223). The tonic cervical reflexes persist after the rigidity has disappeared, although the tonic labyrinthine reflex disappeared as the section passed back of the vestibular nuclei.

The study of the effects of these various transections has made it apparent that there exists a reflex mechanism maintaining a certain amount of constant tonicity in those muscles which counteract gravity. This mechanism keeps the animal in position to move. This tonic mechanism is then modified in various ways by other mechanisms to permit change in attitude or movement. In the thalamus-animal practically the whole of this modifying mechanism is present but much of the mechanism for originating movement is absent. The animal is, therefore, relatively inert but can perform all movements in a coördinate manner. The animal in decerebrate rigidity has lost also practically all of the modifying mechanism, retaining only those elements thrown into action by passive movements of the head. It has no reflex by which the position of the head can be modified. This is constantly retracted. This reflex mechanism for maintaining posture is practically uncontrolled; hence the exaggerated attitude.

When the central nervous axis is transected still farther back, at the posterior extremity of the medulla oblongata just above the first cervical nerve (decapitate animal, Fig. 131 A) all traces of the decerebrate rigidity are usually absent and the four extremities are flaccid, but tonic cervical reflexes can still be obtained (Fig. 130, v). Transection at the fourth cervical level abolishes them. Such an animal is called a *spinal animal*.

The spinal animal has its central nervous system divided into two automatic segments, from both of which various reflex activities can be elicited. Those from the sensory organs of the anterior portion may or may not include the anterior extremities, depending on the level of the section. If we suppose a section at the third thoracic level, after the shock of the transection has disappeared, various reflexes may be elicited involving the hind limbs. If any nocuous stimulus is applied to a hind limb there occurs a flexion of the leg at knee, hip, and ankle. This is usually spoken of as the flexion-reflex. When the stimulus reaches a certain intensity there may occur also an extension of the contralateral hind limb—the crossed extension-reflex. Tickling of the skin of the back causes the hind limb to be brought toward the seat of stimulation in a rhythmic flexor scratching movement—the

scratch-reflex. Pressure on the footpad causes a brief strong extension at knee, hip, and ankle. This is the extensor thrust. These and many other reflex activities of the isolated spinal cord have been studied in detail. But when the bulb has not been severed from the spinal cord, and the condition of decerebrate rigidity exists, these reflexes are modified in very definite ways, just as the presence of the midbrain modifies the postural tone which is so exaggerated when the midbrain is removed. The scratch-reflex is very difficult to obtain and is followed by a rebound and reflex exaggeration of the extension; the crossed extensor reflex and extensor thrust are exaggerated. These results can be explained by the fact that the rigidity in extension is maintained by the stretch-reflex from the rigid muscles and any stimulus tending to reproduce a flexor response must first inhibit the stretch-reflex whereas an extensor-reflex finds itself accelerated.

All of these mechanisms are again modified by the cerebrum and its projection-pathways (300). The spinal cord furnishes the effector mechanism, for the proper functioning of which it is necessary that the animal be lifted from the ground against gravity. The decerebrate mechanism reflexly furnishes the adequate constant tone to the anti-gravity muscles. But it is necessary also that the body be kept in the proper attitudinal relationship when disturbed; the righting reflexes take care of this need. The constant tonic antigravity-contraction is modified by the righting reflexes, and also by cerebral impulses, but immediately resumes its control when these phasic impulses cease. You perhaps understand better now what one means by the hierarchy of function in the central nervous system, although the details of the various complicated reactions I have described will become clear only after careful study.

The recognition of these various conditions in man has been singularly complicated by the assumption of the erect posture, yet some definite facts have been established. By study of the cases of total transection of the spinal cord which occurred during the World War neurologists were able to show that the spinal cord when isolated, and after the initial period of shock has passed, is able to manifest many of the reflex activities characteristic of the spinal animal (405).

The tonic neck-reflexes can rarely be obtained in patients which have a clinical syndrome resembling the condition of the decorticate monkey (68). In favorable cases such a patient (Fig. 132) lies, when the head is in the median plane (A), with elbows semiflexed, fore arms slightly

pronated, and wrists and digits flexed. There is moderate spasticity of all four extremities, the flexors of the arms and the extensors of the legs (plantar-flexors of the ankles) being principally involved. These muscles resist any passive movement at first, then suddenly give way. The

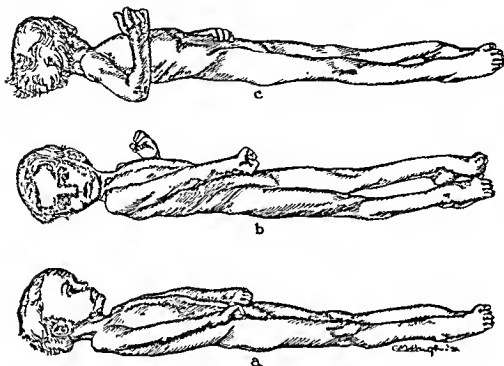


FIG. 132. Tonic cervical reflexes in a child with hydrocephalus (after Draganesco).

limbs have a tendency to remain in any position given them. They are, therefore, plastic to a certain extent but always return slowly to the first described position. The tendon-reflexes are very brisk, with shortening of the muscles after a series of rhythmically induced jerks. A flexor or sometimes dorsal toe-response occurs on plantar stimulation and the leg is withdrawn. When the head of the patient in this state is rotated to the right (B), after a latent period of a few seconds, the right arm is slowly extended at the elbow, the fore arm is still more pronated, but the wrist and digits do not change. The right lower limb may be slowly extended and the foot flexed plantarward. Meantime the left arm is flexed at the elbow, the fore arm is somewhat supinated and nothing happens to the wrist or fingers. The left leg may be flexed slightly at the knee and dorsally at the ankle. The limbs retain these attitudes as long as the head is rotated to the right. When the head is rotated to the left (C) exactly the

reverse movements occur, i.e., the left arm and leg are extended and the right flexed. The movements are usually greater in the upper extremities than in the lower (163).

This condition must not be confused with the cerebellar fits to which we have already referred, in which retraction of the head occurs associated with gross cardiac and respiratory irregularities. These symptoms are due to asphyxia of the bulbar centers (492). Although "cerebellar" fits may be produced by tumors of the supratentorial region, because of herniation of the cerebellar tonsils into the foramen magnum, they are more common with infratentorial tumors. The true condition of decorticate rigidity with tonic cervical reflexes is produced only by supratentorial tumors which compress the brainstem above the tentorium, and thus release the bulbopontine mechanism on which this condition depends, whereas infratentorial tumors compress these centers directly and depress the activity of their mechanism.

The righting reflexes are much more difficult to isolate and demonstrate in man but it has been shown that the act of sitting up in human infants is initiated by a cervical righting reflex (424). After the head is turned to one side, the pelvis is first rotated slightly to the opposite side and then the whole body follows the head, beginning with the shoulders. The infant thus comes on all fours and may progress in this quadrupedal fashion. This method of sitting up disappears after the first years of life in favor of a symmetrical sitting movement but in various pathological cerebral conditions the patient may revert to the primitive method. This reversion is of no importance in localization, however, since it may be found with tumors in many different parts of the brain.

Of the results of all these studies, which have so greatly improved our insight into the functioning of the nervous system, *we must, therefore, isolate the tonic cervical reflexes as the only ones pertinent to our problem because their presence indicates a supratentorial compression of the brainstem.* The patient I have demonstrated to you does not have a complete syndrome of decerebrate rigidity. There are, however, undoubtedly many conditions of partial decerebrate rigidity, the elucidation of which may prove very important for our problem. It is probable that the spasticity of the hemiplegic patient is a partial syndrome of decerebrate rigidity (493) and we begin to understand now that the various associated reactions which we studied in that regard (cf. p. 165) are tonic cervical reflexes acting on the extremity and in

some instances also tonic limb-reflexes acting on the limbs.

After this long digression, which I hope will induce some of you to explore further this fascinating field of neurophysiology, we will turn to pathology for a few moments and discuss briefly the nature of the tumors which provoke such remarkable symptoms. The GROSS APPEARANCE OF A PINEAL TUMOR is not characteristic except for its situation. Hemmed in between the splenium of the corpus callosum above, the brainstem below, and the cerebellum behind, it is usually

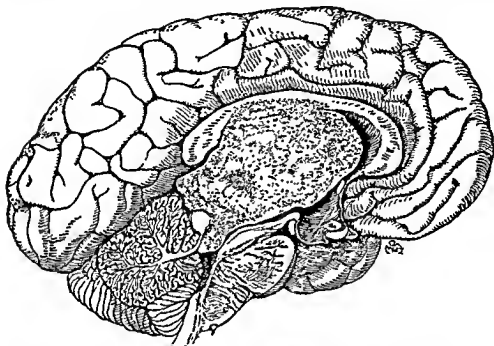


FIG. 133. Median section of brain with pinealoma invading the third ventricle.

quadrilateral in shape unless it invades the third ventricle (Fig. 133). The softer tumors are apt to fill this ventricle completely and add its symptomatology to that of the pineal region. The softer tumors have a tendency also to drop off fragments into the ventricular system which then become secondarily implanted on the walls of the fourth ventricle, third ventricle, or even of the lateral ventricles. In two cases of intense and suddenly appearing diabetes insipidus, such implanted masses were found in the infundibulum of the third ventricle. Rarely a pineal tumor may spread widely in the subarachnoidal spaces, even down the spinal cord.

The MICROSCOPICAL STRUCTURE of the most frequent pineal tumor

is quite characteristic. It is composed essentially of masses of large spherical epithelioid cells (Fig. 134) separated by a network of reticu-

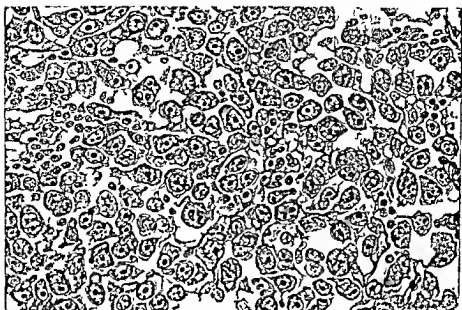


FIG. 134 Drawing of a microscopic preparation of a pinealoma.

lar connective tissue containing numerous lymphoid cells. The epithelioid cells have large spherical nuclei, each of which contains one or two nucleoli and very little chromatin. In their cytoplasm short rods and granules occur in groups. Rarely short stubby processes may be found extending from these cells. There can be little doubt that these epithelioid cells are homologous with the parenchymal cells of the pineal body and their association with a stroma of lymphoid tissue occurs in no other intracranial tumor. Infrequently these tumors may contain small cysts or acini lined by large epithelial cells. These tumors are called pinealomas. In addition, less frequently, there are found tumors composed of a homogeneous mass of smaller cells with smaller nuclei; in these the lymphoid tissue is absent. These latter tumors are reminiscent of the pineal primordium before it is invaded by connective tissue (230). They are distinguished sometimes by such names as pinealomas of spongioblastic type or as pineoblastomas.

The DIAGNOSIS OF PINEAL TUMORS we have already touched upon. They are usually confused with tumors of the third ventricle, tumors

of the cerebellum, and tumors of the brainstem. If *pubertas praecox* is present and the characteristic paralysis of conjugate upward movement of the eyes, the diagnosis is fairly certain. These symptoms, however, are often absent and the diagnosis then becomes difficult or impossible. We have already mentioned that the tumor may spread early into the third ventricle and cause symptoms from this region before symptoms from its primary site arise. The cerebellar symptoms from pressure on the nearby superior cerebellar peduncles may also appear early. They are genuine cerebellar symptoms and differ in no way from those caused by primary cerebellar tumors. But if the ability to look upward were always tested in a neurological examination I am sure fewer mistakes would occur. From the primary tumors of the brainstem the pineal tumors differ rather surprisingly. The tumors of the brainstem cause symptoms of intracranial hypertension late in their development; their first signs are apt to be palsies of the cranial nerves (274); palsies of the third, fifth, seventh, ninth, tenth, eleventh, and twelfth nerves are frequent so that facial weakness, dysarthria, or dysphagia may precede other symptoms for some time; deafness is common but usually unilateral. These patients complain of numbness in their extremities, whereas pineal tumors rarely do so. Hemiparesis contralateral to the cranial palsies is frequent and betrays a primary involvement of the brainstem. From rare tumors of the tectum mesencephali pineal tumors cannot be differentiated clinically.

Often only the symptoms of increased intracranial pressure are present, and even a ventriculogram or encephalogram will only demonstrate an obstruction to the aqueduct which might be only a congenital stenosis. In such cases one can make an exploration or deliberately make a detour around the aqueduct for the cerebrospinal fluid (377).

THE REMOVAL OF PINEAL TUMORS is very difficult (9). They are most often approached from between the parietal lobes (149) by splitting the splenium of the corpus callosum as I did in the patient you have just seen. A successful removal by this method has rarely been reported (244). How many have died from this operation is unknown because failures are not often recorded. Occasionally one may also be successfully approached through a dilated lateral ventricle (481).

CHAPTER 17

MISCELLANEOUS AND METASTATIC TUMORS

SYNDROME OF MENTAL CONFUSION

There remains to be discussed a group of miscellaneous and infrequent tumors which arise within the intracranial cavity, and the unfortunately far more numerous but less interesting group of tumors metastasizing to the brain from distant organs.

INTRACRANIAL TERATOMAS are very rare in the sense of new growths of bidermal or tridermal origin; teratoids are more common (282). Dermoids (394) and epidermoids (271) are also found. They occur most often in the pituitary and pineal bodies, but have been found also in the lateral choroidal plexus, the tela choroidea of the third ventricle, within the substance of the brain, in the region of the tuber cinereum, the cerebellopontine angle and the posterior cistern. They are more frequent in males and are often associated with other congenital malformations of the brain or of other parts of the body, such as spina bifida. They may cause symptoms at any age or are sometimes found incidentally at necropsy. These tumors vary in size from 1-7 cm. in diameter. They are often cystic, the interior being filled with desquamated cells, fatty debris, and hair. Ectodermal structures present in these tumors include squamous epithelium, sweat glands, ganglion-cells, hair-follicles, embryonal teeth, fetal brain-tissue and choroid plexus, sebaceous glands, nerve-fibers, and embryonal eyes. Mesodermal structures include cartilage, smooth muscle, bone, fat, marrow, striated muscle, and lymphoid tissue. Entodermal structures are rarer, the most frequent being epithelium of respiratory or intestinal type with goblet-cells.

One of the most beautiful of intracranial tumors, when exposed at operation, is the so-called PEARLY TUMOR. It is very uncommon; occurring perhaps once in two hundred cases of intracranial tumor. It has a glistening smooth surface and looks exactly like a great pearl against the cerebral tissue. The pearly tumors give symptoms almost always in adult life, if at all. They are often found accidentally at necropsy. Their favorite site is the subarachnoid space over the base of the brain

from the chiasm to the posterior cistern (31). Many have been described beneath the pons and midbrain extending up into the cerebellopontine angle. The gross appearance of these tumors is startlingly like mother-of-pearl. The surface peels away easily from the surrounding structures. The outer layers are tough and malleable like tin-foil. The interior resembles cottage-cheese in color and consistency; it is entirely avascular. These tumors are very irregular in shape, insinuating themselves everywhere between the cerebral and cranial structures.

The microscopical structure of these epidermoid tumors is also characteristic. On the outside is a thin fibrous layer, within which are flattened epithelial cells which sometimes contain granules of keratohyalin. Rarely epithelial bridges can be demonstrated between the cells. Still more internally the cells become more and more polygonal. The central portion is composed of what one might call the ghosts of epithelial cells; their internal structures have disappeared leaving only the shells. This portion resembles the appearance of a dead plant (33). Besides the skeletons and debris of dead cells one finds some fat and usually crystals of cholesterol.

These tumors unquestionably arise from misplaced rests of epithelial tissue within the leptomeninges. Since they have no vascular supply the central portion dies. They are readily removed when they lie in accessible regions of the intracranial cavity since they are soft, avascular, and the capsule peels away readily from the surroundings. They are sometimes found also extradurally under the temporal lobes, within the middle ear, or within the cranial bones.

In about two percent of necropsies, if one examines closely, there will be found on the clivus, about 1 cm. posterior to the dorsum sellae, a slimy excrescence which communicates through a small defect with the interior of the basisphenoid. This small structure goes by the euphonious name of *ecchondrosis physalifera* and has been proved to be a persistent remnant of the notochord. Rarely (about thirty cases have been reported) this structure gives rise to tumors called CHORDOMAS, sufficiently large to cause serious symptoms (39). They may project upward (Fig. 135) and forward into the interpeduncular cistern, into the nasopharynx, or both. Within the intracranial cavity they often extend downward beneath the pons to the foramen magnum. They may extend into the sphenoidal sinuses, the orbits or even into the neck and regional veins. The surface of these chordomas may be reddish but is usually milky white, smooth and grossly nodular. The cut surface

is firm or jelly-like and semitranslucent. There are cysts filled with a mucoid material.

The microscopical structure of a chordoma is characteristic and resembles very much that of the notochord in the embryo. The tumor is composed of cords or masses of large cells with numerous large vacuoles in their cytoplasm. These vacuoles have been shown to contain glycogen. The neoplastic cells sometimes contain more than one

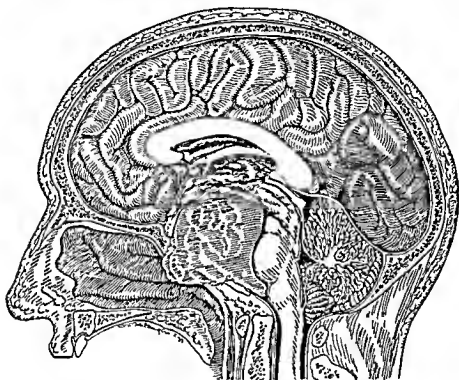


Fig. 135. Median section of head with chordoma.

nucleus. The nuclei are also vacuolated and said to contain glycogen. The cells may be closely packed together but usually are separated into cords or masses by a mucoid material. Rarely cartilage is formed in the tumor and this is sometimes calcified.

The symptoms of these tumors are dominated by numerous palsies of cranial nerves. A moment's reflection on the situation of the tumor will make this understandable. All of the nerves from the optic to the hypoglossal may be involved or any combination of them. Later, compression of the cerebral peduncles may cause pyramidal symptoms

or the compression of the cerebellar peduncles against the tentorium cerebelli may cause cerebellar symptoms. Symptoms of intracranial hypertension may appear but are very late and usually the patient dies before they occur. A very frequent symptom is pain and stiffness of the neck due to extension of the tumor into the foramen magnum.

The diagnosis is often difficult. Whenever multiple palsies of the cranial nerves develop without signs of intracranial hypertension a chordoma may be suspected. In a few instances the erosion of the base of the skull has been demonstrated by roentgenogram. In a few instances also the diagnosis has been established by biopsy of the nasopharyngeal extension of the growth. The intracranial chordoma must be differentiated mainly from the nasopharyngeal carcinoma which has extended intracranially. The latter tumor arises from the epithelium of the auditory tube (of Eustachius) or the pharyngeal recess (of Rosenmueller) and often invades the intracranial cavity before the nasopharyngeal growth is of sufficient size to cause symptoms. In any extensive involvement of the cranial nerves, especially if the involvement is unilateral, a nasopharyngeal carcinoma should be sought. The diagnosis can often be established by biopsy. There is no effective treatment for chordomas.

In the lateral ventricles and in the roof of the third and fourth ventricles PAPILLOMAS (165) may arise from the tangled masses of bloodvessels surrounded by neuro-epithelial cells which are known as the choroid plexuses. They are rare, constituting not over 0.5 per cent of intracranial tumors, occur most frequently in the first decade of life and diminish in frequency with each succeeding decade. They are most commonly located in the fourth ventricle, less frequently in the lateral ventricles, and rarely in the third ventricle. Those from the plexus of the fourth ventricle may arise from the tuft projecting through the lateral foramen (of Luschka) and hence lie primarily in the lateral cistern.

When these papillomas do not fill the ventricles entirely their gross appearance may be quite characteristically granular, but sometimes they seem to be covered by a thin capsule so that the surface is smooth. The cut surface, however, is always granular and often contains numerous small cysts. The tumor may completely fill the ventricle and obliterate its wall. In other cases the ventricles become greatly dilated although they are not obstructed (Fig. 136). It is difficult to explain how this comes about. The hydrocephalus in these

cases is usually attributed to hypersecretion of the plexuses. We have already seen that the cerebrospinal fluid is probably not a secretory product. The hydrocephalus may be simply a concomitant, independent process. It does not always accompany papillomas. In rare cases fragments of the papilloma may become free and implant themselves on

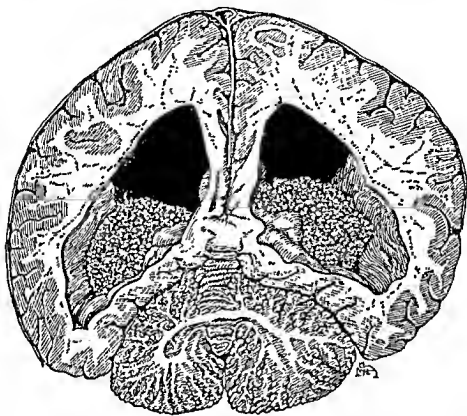


FIG. 136. Papilloma of the choroid plexuses of the lateral ventricles (after Davis).

the walls of other ventricles or in the subarachnoid space. The microscopical structure is that of a typical papilloma. The cores of the papillae are composed of small bloodvessels surrounded by a little connective tissue. The covering epithelium is pseudostratified and columnar in most cases. The cells are elongated with oval nuclei. Numerous mitochondria are present in the cells but no blepharoplasts, and the cells are not ciliated.

There are no characteristic diagnostic signs. The fact that the tu-

mor is near or in the ventricle may be suspected from examination of the cerebrospinal fluid; in some instances it has been yellow with a greatly increased content of protein. These growths are rarely calcified. A tumor in the cerebral hemisphere of a very young infant is most likely to be of this type. Treatment is difficult. A few such tumors have been removed (483); from the fourth ventricle it is relatively easy, from the others more hazardous. Roentgen-radiation decreases their vascularity and makes their removal easier.

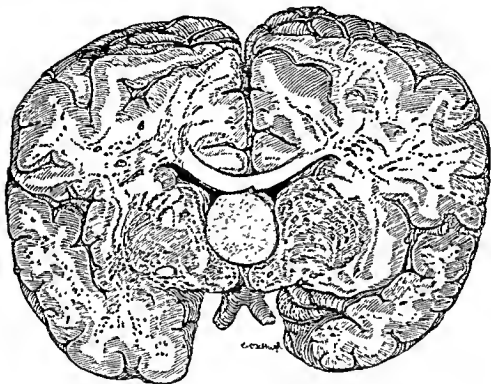


FIG. 137. Cross section of brain with colloid cyst in the third ventricle (after Wilson).

In the third ventricle occurs a strange COLLOID CYST closely allied to the papilloma (220). It is always situated at the anterior extremity of the ventricle between the interventricular foramina and attached to the roof (Fig. 137). It is round, with a smooth surface, although there may be on its inferior surface a few small tufts of choroid plexus, about a centimeter in diameter and of the consistency of a soft rubber ball, at least after fixation in formalin. The interior of the ball is filled with a homogeneous colloid material containing some cellular debris. The

wall is composed of a layer of epithelial cells surrounded by a capsule of connective tissue. These colloid cysts probably develop from the primordium of the paraphysis, which in lower vertebrates is a ramified epithelial structure arising from just this anterior extremity of the roof of the diencephalon. In the human embryo this structure is very transitorily present. Such an origin would explain the unique situation of these tumors. There is no way of making a positive diagnosis of such a tumor. The presence of an intraventricular tumor may be suspected by the intermittent progress of symptoms, which is very frequent, suggesting an intermittent blocking of the circulation of cerebrospinal fluid.

The frequency of this intermittent clinical course in these cases is really astonishing. I am able to show you a specimen (100) of this unusual tumor (Fig. 137). You see it lies just as I described it to you. The patient (CASE XLIII) *was an apparently healthy woman of fifty-one years who came home one evening complaining of headache, was nauseated and vomited. The headache increased in severity, the vision became clouded, and early next morning she became comatose. The respirations became slow and labored and she shortly died. On inquiry it was learned that about the age of eighteen she had such an attack, her vision was impaired, and she was told she had a retinal hemorrhage. At the age of forty-one the headache suddenly reappeared accompanied by nausea and vomiting. For nearly three months the headache persisted. After coming home from work she would lie down and sleep the entire evening. She was drowsy during the entire day also. After three months the symptoms disappeared entirely for nine years, only to recur as I have described. Postmortem examination revealed nothing of significance outside the cranial cavity. There was slight dilation of the lateral cerebral ventricles and this firm colloidal ball between the interventricular foramina.*

In discussing the meningeal tumors I mentioned that rarely LIPOMAS develop in the pia mater. The dorsal surface of the corpus callosum seems to be a favorite site for them, and the tuber cinereum and midbrain are also frequent sites. They are rare tumors, constituting not more than 0.5 percent of all intracranial tumors. Most of these tumors are composed of fully developed fat-cells, but some contain more embryonic cells and resemble in structure the xanthomas. They are sometimes associated with malformations of the brain, especially defects of the corpus callosum. Most of the lipomas do not cause symp-

toms and are found incidentally at necropsy. There are many theories of their origin (475): (1) that they arise from lipid cells already present in the pia mater; (2) that they arise by fatty transformation of the connective tissue; (3) that they arise by "dedifferentiation" of the pial cells toward an embryonic form with a subsequent metaplasia into fat; (4) that they arise from embryonal remnants. This multitude of theories is an indication that these tumors are very interesting to the pathologist because of their bearing on the problem of the genesis of tumors in general. They are too infrequent to be of much importance in the clinic.

We have, unfortunately, to deal not only with tumors developing primarily within the intracranial cavity but also with metastases from tumors in distant organs. Since INTRACRANIAL METASTASES may give symptoms before the primary tumor it behooves us to be on the lookout for such cases, and a knowledge of those tumors which commonly metastasize to the brain is a great aid in detecting the often minute primary focus. I want to show first a patient in whom the primary lesion is obvious, principally because her mental condition is rather characteristic of multiple metastases in the brain.

A housewife (CASE XLIV) of fifty-seven years entered the clinic complaining of terrific pains in the head, at times occipital, at others temporal, sometimes over the eyes, of four weeks' duration. The headache came in waves and during this time she held her head and groaned. During the headaches also she was confused and seemed not to comprehend what was said to her. Two weeks after the onset she became semi-comatose, thrashed about apparently in great pain and vomited several times. A lumbar puncture was made at this time; the spinal fluid was under great tension. After the puncture she was better for a while, but the headaches renewed their intensity, she again became confused, and was brought to the hospital.

She had been ailing or apprehensive of illness most of her life but it was not until three years ago that anything occurred which might have a bearing on her present trouble. She then discovered a sore spot in the right breast above the nipple. A diagnosis of carcinoma was made, the breast was removed and the diagnosis confirmed by microscopical examination of the lesion. Roentgen-radiation was given every month for the succeeding eleven months. Two years later she began to complain of a feeling of fullness in the right side of the abdomen. She passed some blood in the stools but was told it came

from hemorrhoids. She developed a stubborn diarrhea and became very nervous and apprehensive of a spread of her cancer. She would have spells of a panicky feeling in which she thought she was going to die. During these spells she thought she could not focus on anything, kept taking off her glasses, and said she felt queer in the head. A month later the left eye became sore and looked bloodshot. A small growth was found in the lower lid; it was removed and found to be carcinoma. She complained also of pain in the spine and in the left ankle. Roentgenograms of head, spine, and lungs were taken and disclosed nothing abnormal, but still she insisted something was wrong in her head. Finally a few weeks ago began the symptoms of acute intracranial hypertension.

On admission she was moaning with pain and very confused. She did not know where she was and did not recognize any of the people around her. She did not cooperate at all in her examination. She complained that her head ached and was greatly annoyed by the attentions of her physicians. There was a scar of a previous mastectomy on the right side of the thorax, but no evidence of local recurrence or of involvement of regional lymph-nodes. On general examination no evidence of any metastases was found in the abdomen. The optic discs were choked about one diopter, with hemorrhages in both retinæ. There was a slight left lower facial weakness and occasionally a tendency toward an extensor plantar reflex on the right side. Otherwise the neurological examination was entirely normal. Roentgenograms of the head, chest, and pelvis, revealed only one small metastatic lesion in the left occipital region of the skull.

She was given 50 ccm. of a solution of 50 percent glucose intravenously. This improved her condition sufficiently so that she ceased to resist examination and ceased complaining of pain in the head. *She would carry out simple commands but it seemed a great effort to comprehend them.* She recognized her husband but did not know where she was or what time it was. Her attention wandered readily. She would make meaningless remarks at times in reply to a question. This morning she evidently is delirious and you hear that she talks about objects on the ceiling and now and again points apprehensively upward and cries "Look out for those chains." Again she suddenly looks startled and says "Who is that lady over there?" pointing to the nurse. She points to me and says, "Look out! You will drop that chair." She talks a great deal in a low mutter, making totally unconnected

statements. I catch, when she raises her voice, for example, "She got the ironing done, didn't she?"

There is no doubt that this woman is suffering now from multiple metastases. One probably has lodged in the occipital bone; another was removed from the left lower eyelid. There are doubtless others which we have failed to demonstrate and in particular multiple foci in the brain. I have shown her largely for the mental symptoms, which are those of MENTAL CONFUSION. When she entered, the mental condition might be taken for that of acute intracranial hypertension and yet there were differences, for example it was impossible to get her into contact with her environment even with the strongest stimuli. This morning there is no further doubt. The intracranial tension has been reduced so that she no longer complains of headache and gives no sign of discomfort, yet her confusion is all the more apparent. The mental condition is that of a diffuse insult to the brain and as such is seen in intoxications, severe exhaustions following infectious diseases, following trauma, low-grade meningitis or encephalitis. It is also produced by multiple metastases in the brain in which this sudden development of mental confusion occurs frequently.

Confusion is the characteristic reaction of the normal brain to a general insult. In acute or subacute intoxications it takes the form so familiar from alcohol and known as delirium tremens. The patient has an anxious or terrified look, perspires and trembles. The reason is not far to seek, for he lets it be known that he is a spectator and actor in a dreamworld in which he sees multiple, moving, often terrifying objects. His usual reaction is to flee from these visions. In milder cases, or in patients recovering from delirium tremens, it is possible to suggest terrifying objects which the patient then sees and is frightened by. Often the hallucinations are not terrifying and have to do with such things as the patient's profession. Olfactory, gustatory, and tactile hallucinations are sometimes present, rarely auditory. The other frequent form of this mental syndrome of confusion is the torpor of the postinfectious states. The torpor varies, however, and sometimes gives way to periods of delirium, and all possible transitions are observed. When well developed this condition is marked by an intellectual, motor and affective inertia. The patient lies flat, with a vague and expressionless face. He is inattentive and seems not to think. He does not worry about his condition, does not inquire about his relatives, or show any affection when they are present. He shows

evidence of tremendous effort when an attempt is made to get him to respond. To persistent questions he rouses with difficulty, looks dumbfounded, asks that the question be repeated, wrinkles his forehead, and puts his hand to his head with an impotent gesture. Any response he makes comes slowly and incompletely. The effort seems to exhaust him and he soon falls back into his former inattentive attitude. The replies it is possible to obtain make it evident that he is

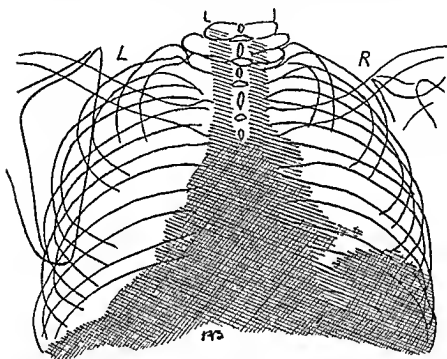


FIG. 138 Scheme of roentgenogram from CASE XLV. Atelectasis of the lower lobe of the right lung from bronchial carcinoma. Compare Plate IX.

disoriented, that his perceptions and ideas are obscure. A haze seems to be over his mind which he struggles to penetrate. When the torpor is less pronounced the patient recognizes objects and persons falsely. In its complete form mental confusion is rarely encountered in cases of intracranial tumor, except with multiple metastases or with very accentuated intracranial hypertension, but milder degrees of the syndrome are often present.

The second patient (CASE XLV) has no marked mental symptoms. She may have more than one metastasis in her brain, but the symptoms

can be explained on the basis of a single large one. She is a housewife of fifty-one, always well and strong except for a short period of pain in the right upper quadrant of the abdomen accompanied by jaundice. This was cured by cholecystectomy. She began eight months ago to suffer from dull headache which varied in intensity but recurred practically every day. She never vomited. About four months prior to admission her right arm and leg began to grow weak. Suddenly there occurred a right-sided convulsion accompanied by pain in the right side of the face. It was difficult for her to talk for half an hour after the convulsion and the right side of the body was numb.

When admitted to the hospital she was mentally alert and oriented. There was no evidence of aphasia. There was a lower right facial weakness and a right hemihypesthesia. Stereognosis was normal. There was a right spastic hemiparesis with clonus at the right ankle and an extensor plantar response. There was no choking of the optic discs and no defect in the visual fields. There was no evidence of cardiovascular disease. No history of syphilis could be obtained and the serological reactions of the blood were normal. Roentgenogram of the head was normal except that the pineal body could be seen to be shifted 1.5 cm. to the right of the midline. A diagnosis of infiltrative glioma of the left parietocentral region was made.

An osteoplastic operation was performed a week ago in the left parietal region. It disclosed a large tumor which reached the surface about the middle of the posterior central gyrus and contained a ragged cavity filled with dirty yellow fluid. The tumor infiltrated the brain in every direction. Part of it was removed and the wound closed after leaving a decompression in the temporal region. The patient has recovered promptly but the right hemiparesis is much worse and there is now an aphasia as well which is, however, improving.

Microscopical examination of the neoplastic tissue removed showed it to be carcinoma. A search was then begun for the primary source of the tumor. Careful physical examination again failed to reveal any neoplasm, but roentgenogram of the lungs discloses a primary bronchogenic carcinoma of the right lung with partial atelectasis of the lower lobe (Fig. 138). Persistent questioning of the patient and of her relatives has failed to find any symptoms relative to the lungs. This story is entirely typical. *Primary bronchogenic carcinoma of the lung (10) so commonly metastasizes to the brain, and does it so often before the primary tumor has given symptoms, that it should always be looked*

for in any patient of middle age, or beyond, who develops rather rapidly symptoms of an infiltrating tumor of the brain, especially if the signs of intracranial hypertension are not marked or there is a pronounced mental confusion.

Carcinoma of the lung seems to be increasing in frequency and constitutes now 7 to 10 percent of all carcinomas. It develops usually from forty to sixty-nine years of age, almost always from a primary bronchus or one of its early divisions (217). It enlarges the bronchial wall for a short distance and then spreads into the surrounding pulmon

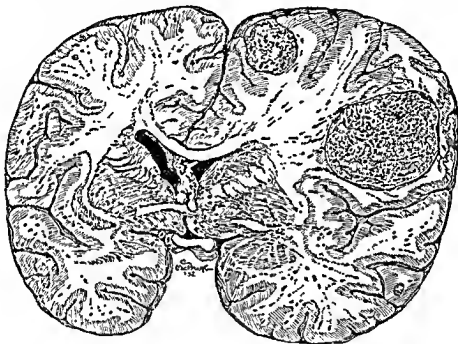


FIG. 139. Transverse section of brain with multiple carcinomatous metastases.

ary tissue in fine branching projections. It usually develops near the hilum; the regional lymphatic nodes are early involved. Small regional metastases are often found in the same lung or that of the opposite side. In the brain a single nodule may be found, but most commonly numerous metastases are present. These must reach the brain by way of the arteries as emboli. In this way may best be explained the sudden onset of cerebral symptoms in many cases.

The metastases exist as firm enucleable masses (Fig. 139). The

centers of the masses become necrotic after a certain size is reached. The cavity contains a dirty, dark yellow, or greenish fluid filled with debris, phagocytes, and cholesterol. In microscopical structure the metastases resemble the original tumor. The ventricles of the brain are rarely dilated in these cases, but there is often a tremendous edema of the brain so that the intracranial tension is out of all proportion to the mass of neoplasm present. The surrounding cerebral tissue is usually just pushed aside. Near the nodules there may be clasmatodendrosis of the neuroglia, transformation of the microglia into scavenger cells, swelling of the oligodendroglia, acute swelling of the neurones, and fragmentation of the myelin-sheaths, but for the most part one finds only compression of the neighboring tissue and edema of more distant parts.

Recently it has been supposed that carcinomatous metastases reach the brain by way of the anastomotic veins described by Batson (61). This theory is illogical since one would expect them to follow the most direct and shortest route from the lung into the spinal canal where they are rarely found and, if they spread by this route to the intracranial cavity, that they be found in the venous sinuses and meninges; on the contrary, they are almost invariably found as discrete nodules deep within the brain. Nevertheless, in rare instances they do get into the meninges and spread widely to form what is called a carcinomatosis of the meninges (247). That is what it did in this woman (CASE XLVI) of forty-three who was always well until six months ago when she began to suffer from headache in the parieto-occipital region. It was present most of the time, especially at night. Early in the morning she would awake with the pain, would be nauseated, and vomit; then she would feel relieved for a time. Movement of the head would increase the pain. When examined two months after the onset the optic discs were choked two diopters but there was no hemorrhage in the retina. There was a questionable right extensor plantar reflex at that time but no other findings. Vision at that time was perfect but began to fail about a month later. She began at this time also to have sharp shooting pains in both eyeballs.

When admitted to this hospital a month ago she was oriented and had no mental disturbance except that her memory for recent events was somewhat poor. The tendon-reflexes were everywhere very weak and could be elicited only by reinforcement. There was a coarse tremor of the outstretched hands. At times there was obtained an extensor plan-

tar reflex on the right side. There was otherwise no evidence of involvement of the nervous system apart from the eyes.

The fundus of the right eye was uniformly clouded and so opaque that the choroid coat was not visible. The margins of the optic disc were very indistinct; the disc itself was grayish, elevated three diopters, and seemed twice its normal diameter. None of the large retinal vessels was visible over the optic disc, but there were numerous capillary vessels. The arteries seemed somewhat constricted, the veins of normal caliber. Numerous flame-shaped hemorrhages radiated out from the disc in every direction. Below the disc these hemorrhages covered most of the retina. In the macula were numerous tiny globes of hemorrhage. Between the macula and the disc were yellowish-white streakings as in albuminuric retinitis. The left fundus was largely obscured. The disc was hazy and indistinct, but elevated only one diopter. The superior and inferior retinal veins could be seen over the disc but were obscured near its margin. The disc was surrounded and encroached upon above and below by areas of massive hemorrhage radially striated. Nasally the hemorrhage was less dense. The retinal arteries, where visible, seemed slightly constricted; the veins were normal. The macula was heavily pigmented and between it and the disc were small white blotches. The patient was practically blind, but still able to distinguish light with the right eye. The ophthalmological diagnosis was bilateral hemorrhagic neuroretinitis.

The most careful search failed to reveal any cause for the retinal condition. Roentgenogram of the skull revealed vague decrease in density of the inner table in the left parietal region and also in the right posterior frontal region but nothing definitely pathological. There was no evidence of renal disease and no Bence-Jones protein in the urine. The systolic bloodpressure was 130. The erythrocyte-count was 3,900,000. The erythrocytes were pale, with many anisocytes and much basophilic stippling. There were also numerous immature polymorphonuclear leucocytes and a definite eosinophilia, a few myelocytes and possibly myeloblasts. The findings in the blood indicated stimulation of an exhausted bone-marrow. Cultures of the blood were sterile. The temperature, which was elevated on admission, subsided promptly after the opening of a perirectal abscess. It was determined to investigate the suspicious areas of the skull. A button of bone was, therefore, removed with a crown-trephine from the right frontal region. The bone appeared normal, as did also the dura mater, but on the

under surface of the dura mater was a layer of reddish-gray tissue about 1 mm. in thickness, a portion of which was removed for examination. The ventricle was punctured; the cerebrospinal fluid was found to be normal and under no tension. Examination of the subdural tissue showed it to be carcinoma. An exhaustive search has failed to reveal the primary tumor but roentgenograms of the other bones disclose areas from a few millimeters to 2 cm. in diameter of decreased density, surrounded by increased density, in the ribs, right humerus, and pelvic bones. They are interpreted as due to multiple carcinomatous metastases.

✓ When carcinoma invades the meninges primarily it may spread either in the subdural or subarachnoid spaces. It rarely involves the brain directly. These membranes behave rather passively in the presence of the invader. The carcinomatous cells multiply in the meshes but soon die, and their remains are carried away by macrophages. Intracranial carcinoma is always a secondary process. It usually reaches the brain by way of the arteries, but the meninges are involved most often by direct extension or possibly along the trunks of the cranial nerves. *One of the most frequent sources of such invasion is the nasopharynx (521).* A characteristic clinical picture is produced in these cases, as illustrated by the following patient.

This man (CASE XLVII) of forty-five years was well until ten months ago when he began to suffer from intermittent pains in the head radiating from the right eye to the back of the neck. Shortly afterwards he noticed a discharge with disagreeable taste which came down from the nose into the throat. A month later the pain in the right eye became constant and he saw double. His hearing gradually failed. He lost fifty pounds in weight.

When admitted to the clinic a month ago there was found a ptosis of the right upper eyelid and impaired movement of the right eyeball in all directions except nasally. Visual acuity was normal in both eyes. The pupillary reactions were normal and the fundi also. There was a weakness of the right seventh nerve of peripheral type. The palate was weak on the right side. Auditory acuity was diminished in the right ear. There was a slight weakness of the right pterygoid muscle and of the right trapezius muscle. The voice was hoarse but the vocal cords could not be seen. The neurological findings were thus confined to the cranial nerves on the right side. General examination disclosed a fibrous tuberculosis of the apex of the left lung and en-

largement of the lymphatic glands in the right side of the neck. An ulcerated mass was found in the right nasopharynx. Biopsy proved the mass to be carcinoma; a yeast was obtained from the ulcer. The patient was given intravenous injections of sodium iodide. The enlarged glands in the neck have after three weeks largely disappeared and may have been merely inflamed. There is now a complete external and internal ophthalmoplegia of the right eye.

In this patient the nasopharyngeal tumor was readily found but when such tumors arise in the peritubal region they rarely cause at their onset an ulceration or appreciable tumor in the nasopharynx. Even examination after cocaineization may not reveal it. The patient usually presents himself with apparently an ordinary rhinopharyngitis, with or without otitis media, and is so treated until involvement of the cranial nerves occurs. Very often there are no nasopharyngeal symptoms at all. The tumor develops along the auditory tube (of Eustachius) and penetrates into the skull usually through the foramen lacerum. The trigeminal nerve is encountered early and may long be the only nerve involved. Slight deafness is also an early symptom but is caused by blocking of the auditory tube. The invasion of the trigeminal nerve causes dull continuous pain, first in the lower branches and later in the ophthalmic branch. The nerves are tender to pressure at their exits from the skull. The motor branch is paralyzed early. Later the pain is accompanied by anesthesia. The cornea of the corresponding eye becomes anesthetic and ulcer may develop. Soon the nerves of the eyeball are caught. In some cases the ocular palsies may precede the trigeminal symptoms. First the abducens is involved, causing an internal squint, and later the third and fourth nerves, so that a complete internal and external ophthalmoplegia is the final outcome. The cerebellar fossa is rarely invaded. The seventh nerve is usually involved outside the cranium. The ninth, tenth, and eleventh nerves are not infrequently caught in the jugular foramen. The symptoms are all unilateral. There is rarely any intracranial hypertension, the tumor spreading mainly outside the dura mater. Aside from the characteristic clinical syndrome the diagnosis may be established by biopsy of the nasopharyngeal tumor or sometimes of the lymphatic glands at the angle of the jaw which are almost always involved at some period of the tumor's development.

Arising in the same situation, and causing the same symptoms, a lymphosarcoma may invade the cranial cavity in exactly the same

way. Sarcomas do not give rise to intracranial metastases as commonly as carcinomas, but when they occur they do so apparently in exactly the same manner. By direct extension the tumor may get into the meninges and spread there to form a sarcomatosis of the meninges.

Finally, I should like to show you an interesting brain of a formerly healthy workman (CASE XLVIII) thirty-eight years old, who began to feel tired about five months before his death. He complained also of some frontal headache over the eyes. There were no symptoms until three months later when he began to vomit. Since then the headaches increased and vomiting was more frequent. He was obliged to cease work and come to the hospital for relief.

When admitted he was inattentive and indifferent. He did not coöperate in his examination and answered questions at random and in monosyllable. His head was large and square. His right eyeball was absent, said to have been removed three years previously after injury by a blowpipe. The left optic disc was choked about four diopeters. There was pain in the neck on flexion of the head. There was a right lower facial paresis and the grasp of the right hand was weak. The right abdominal and cremasteric reflexes were absent. There was clonus at both ankles and bilateral extensor plantar reflexes, more easily elicited on the right side. The tendon-reflexes were brisker on the right side. Because the patient's condition made proper examination impossible and the findings were not clear, air was injected into the ventricles. A roentgenogram showed that the anterior extremity of the right lateral ventricle was flattened and pushed upward and that the entire ventricular system was displaced to the left. There was evidently a large tumor deep in the posterior part of the right frontal lobe. It was judged to be inoperable and a subtemporal decompression was made. The patient continued very weak and semi-comatose for a few days, then developed symptoms of hypostatic pneumonia and died.

A necropsy was performed one hour postmortem and revealed atelectasis and bronchopneumonia of the lower lobe of the left lung. In addition, in the middle lobe of the right lung was found a tumor-nodule of soft pinkish tissue 3x2 cm. in diameter. At the base of the lower lobe was another similar nodule 2x1.5 cm. Nothing else of importance was found in the general examination. In the brain was found in the posterior inferior part of the right frontal lobe a large tumor measuring 5x4 cm. (Fig. 140). It was dark brown in color and sharply circumscribed. It pushed the right lateral ventricle upward

and flattened it. The basal ganglia on the right side were pushed backward. The left lateral ventricle and the posterior part of the right ventricle were grossly dilated. Microscopical examination of the tumors showed them all to be melanoblastomas.

Later investigation disclosed that the eye when removed was not examined even grossly. The ophthalmologist admits that there might have been a primary tumor in the eye. His office-notes state that at his first examination he found a detachment of the retina. Four months later there was a more marked detachment, higher intraocular tension and pain in the eyeball. These findings are compatible with a primary melanoblastoma of the eye.

Melanoblastoma of the eye develops in the choroidal coat, in patients usually from forty to sixty years of age. It manifests itself first

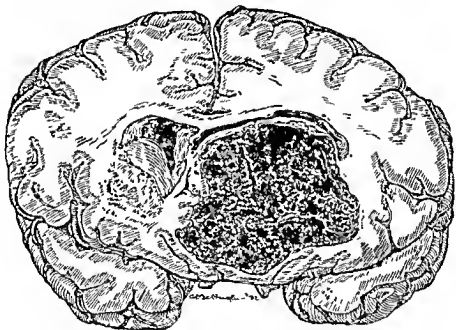


FIG. 140. Transverse section of brain from CASE XLVIII with metastasis from melanoblastoma of the choroidal coat of the eye.

only by detachment of the retina and the resultant defect in the visual field. Later comes a complete detachment of the retina and blindness of that eye. Still later the intraocular tension rises and the condition resembles that of inflammatory glaucoma. There is marked injection of the eyeball, clouding of the cornea, discoloration of the iris, dila-

tation and fixation of the pupil, clouding of the lens, and high intraocular tension. At this stage the eye is very painful and it was doubtless at this stage that the eyeball of our patient was enucleated. If enucleation is not made the tumor soon breaks out around the circumference of the cornea or backward along the optic nerve and invades the orbit. Finally it follows along the optic sheath into the brain or involves the regional lymphatics and is carried to more distant organs, most frequently the liver. Even though enucleation is made early, before the tumor ruptures into the orbital tissues, metastasis may already have occurred.

Other tumors of the eye may also metastasize to the brain, notably the gliomas of the retina. They occur mainly in children under five years of age. Sometimes more than one member of a family has the malady. Both eyes may be involved. These tumors develop in the same stages as the melanoblastomas of the choroid coat. There are two main varieties, the retinoblastoma and the neuro-epithelioma (235). The former is the more malignant. When detachment of the retina occurs the tumor may be hidden, but even at this early stage the presence of a tumor may be established by a determination of the percentage of glucose in the fluid behind the detached retina. It is of primary importance to establish the diagnosis early before metastases have occurred.

It is difficult to obtain exact figures on how often different types of tumor metastasize to the intracranial cavity. It is usually stated that sarcomas more often metastasize to the brain than carcinomas, yet this is not my own experience nor that of many clinicians of wide experience with whom I have spoken. The high percentages given for sarcoma probably arise from the inclusion of melanoblastomas in this group. Melanoblastomas of cutaneous origin metastasize freely to the brain. Certainly everyone is agreed that pulmonary carcinoma frequently metastasizes to the brain even before any pulmonary symptoms develop. Perhaps in as many as 30 percent of cases such metastases occur (229). Mammary carcinoma also frequently, perhaps in 5 or 6 percent of cases, forms metastases in the brain but in this case the primary growth is readily located. Nearly half of the melanoblastomas metastasize to the brain. Hypernephroma lags behind with 7 or 8 percent. Statistics indicate that metastases to the brain from malignant tumors will be found in about 0.5 percent of necropsies. The percentage of primary neoplasms of the brain is perhaps 1 percent of all necropsies.

This would indicate that of all intracranial neoplasms, both primary and secondary, metastases constitute perhaps 33 percent. In neurosurgical statistics the percentage of metastatic tumors is only about 4 percent since usually only those are sent to the surgeon in which the primary source has not been discovered. My impression is that both figures are incorrect. Metastatic tumors are surely more frequent than 4 percent, and probably less numerous than 33 percent, of the total of all intracranial neoplasms. In the Leeds General Infirmary they were found in 17 percent of the cases (225).

The symptoms of metastatic cerebral tumor, as the foregoing histories indicate, do not differ essentially from those of primary cerebral tumors. We have noted as more or less characteristic simply the intensity of the headache and of the mental confusion, which are out of proportion to the intracranial tension. The DIAGNOSIS of metastatic tumor, therefore, depends in most cases on the recognition of a primary tumor elsewhere. We should insist again, however, upon the frequency of pulmonary cancer which metastasizes to the brain before pulmonary symptoms develop and before the primary tumor can be detected by physical examination. Any patient in middle age or older who develops suddenly a psychosis or focal cerebral symptoms, not obviously luetic or vascular in origin, should have a roentgenogram made of his lungs.

The TREATMENT of metastatic malignancy is, of course, very unsatisfactory. When recognized as such, an intracranial operation should rarely be undertaken because the metastases are usually multiple. When focal epileptic attacks indicate a cortical nodule it may be worth while to operate on the chance that there is an isolated tumor. Decompression is not advised because the relief afforded lasts but a short time. Roentgen-radiation is ineffective and dangerous because of the already existent, often intense, edema of the brain. The establishing of the correct pathological diagnosis will save much futile operating in these cases. Operations to stop pain in malignant cases by section of the sensory roots of cranial nerves are always permissible (189).

CHAPTER 18

GENERAL DIAGNOSIS

SYMPTOM COMPLEXES OPHTHALMOSCOPY VENTRICULOGRAPHY

Heretofore I have tried to present sharply defined syndromes characteristic of the various pathological types of tumors in different locations in the intracranial cavity. Such a procedure is necessary as an introduction for the student. But I should serve you very ill if I left you with the impression that the situation is always so clear. We have now to consider some of the difficult problems common to all intracranial tumors. *The first step toward establishing a diagnosis of intracranial tumor is to have the possibility of its presence occur to the physician.* How often do patients remain in the care of a physician for weeks or months before this possibility occurs to him! Yet there are certain symptoms which should invariably suggest to the physician the possibility of intracranial neoplasm. Repeated bouts of headache, for example, are often passed off as migraine. We cannot, of course, say that migraine is a definite disease yet the symptom-complex which goes by this name has certain definite, though vague, characteristics in the absence of which the diagnosis should be accepted with caution.

Migraine has a very definite hereditary background. The patients are active and excitable, and in a large percentage of cases (variously estimated from 50 to 80 percent) either the father or mother, or both, suffered from the same complaint. The malady has been traced in certain instances through several generations. The onset of the disease occurs usually anywhere from the age of ten to forty years, rarely later, the vast majority beginning before the age of thirty. Migraine has a close relationship to epilepsy and many migrainous patients later develop convulsions (185).

In the simpler types of migraine the patient feels mildly depressed for a day or so before the attack, with the aimless psychomotor unrest which sometimes accompanies this mental state. He cannot keep his mind on his work; his head feels heavy and his mind dull, and he is generally unproductive. After a day or so of this he wakes in the morning with a headache. With the onset of the headache, or even before, there begins usually nausea which increases in intensity and

ends in vomiting. Loss of appetite or even distaste for food is common and may exist in the absence of much nausea. In the milder attacks during which the patient is not completely prostrated, he is nevertheless still depressed, lax, and dull. There is often a hyperirritability of the special senses so that the patient cannot tolerate bright light, loud noises, strong odors or tastes. Scintillating scotomas occur and even ophthalmoplegias or hemianopia. Generally an attack begins in the morning and after a crescendo of varying intensity disappears toward evening. The patient then sleeps soundly and the following morning feels quite well. More rarely attacks may last only two or three hours or even extend two or three days. The attacks rarely occur oftener than three times a month, usually at intervals of two to four weeks.

In such more or less typical cases of migraine with definite hereditary basis and onset in youth little difficulty will arise. But the headache which accompanies many intracranial tumors, especially ventricular tumors, is intermittent and may be accompanied by visual phenomena and transitory palsies. Any case of intermittent headache, occurring first in adult life, and especially if no history of familial taint can be obtained, should be suspected and an ophthalmoscopic examination repeated at frequent intervals. And it should not be forgotten that a migrainous patient can develop an intracranial tumor. I have often obtained a history that the patient suffered from sick headaches all her life. In a patient with migraine any sudden change in the phenomena of the attacks or any undue increase in frequency or severity should put the physician on the alert. Stupor, slowing of the pulse, papilledema, or any other symptom of intracranial hypertension or any tendency of the palsies to become permanent should provoke a thorough investigation at once.

I shall tell you of some patients suffering from RECURRENT HEADACHES. You will then appreciate better the difficulties of diagnosis in these cases and the necessity of caution in dealing with them. The first is a young woman (CASE XLIX) whom I cannot show you for obvious reasons. She was well until about New Year's day, 1930, when a severe headache in the frontal region occurred. It felt as if her "head were held in a vise." The headache lasted only half an hour and left her weak. Similar headaches recurred at intervals of three or four weeks until July, 1930. They lasted a few minutes or half an hour. There was no vomiting but they left the patient weak and tired. In July the headache began to be associated with nausea and vomiting.

Moreover, movements of her head would cause dizziness and a sensation as though the contents of the head were moving. Since July the patient had lost twenty or thirty pounds in weight. For the last two months there had been pain in the eyes, especially the right. The last headache had occurred five days before admission to the hospital. It had come on early in the morning and lasted all day and the following night. It was much worse on lying down. It quieted somewhat when she sat up, but just as soon as she attempted to lie down another sharp pain would come in the frontal region over the eyes which would bring her up again screaming with pain and holding her head. She was nauseated and vomited several times.

When she was admitted to the hospital practically nothing was found. She was thirty-one years of age, much worried and apprehensive, but intelligent and perfectly oriented. In talking with her one got the impression that she was intensely afraid of something. She repeatedly remarked "I hope I get out of this place all right." As she told her story one got the impression also that the description of the headaches was overdrawn. Likewise her fear of changing position seemed exaggerated. She would rise slowly in bed and then lower herself very gently and gradually, not because of pain, for she had no headache at the time but, as she said, for fear of pain or of queer rushing sensations in the head. Nothing was heard in the head during change of position and she was repeatedly and rapidly changed from sitting to lying position without causing any discomfort. She was undernourished and weak; her systolic bloodpressure was only 100. In addition a few nystagmoid jerks of the eyes on looking to the left were observed and the abdominal reflexes were not obtained; that was all. Once or twice there seemed to be some slight tendency to deviate to the right when walking. She had one slight headache while in the hospital, during which the nystagmus became more definite, not only to the left but also to the right and upward. The optic discs and fields were quite normal. Hearing was normal and the vestibular apparatus functioned normally on both sides. The dentist could not even find any infected teeth nor the rhinologist any chronic sinuses. She was examined carefully for tuberculosis but none was found.

Her husband was informed that we were unable to make a diagnosis. There was no history of migraine in the family and the attacks of headache were of recent origin; so we strongly suspected tumor, and advised making a ventriculogram. The patient flatly refused. Since

she lived nearby, the husband was told to take her home and bring her back immediately at the onset of a bout of headache. The headache did not recur for nearly a month. The husband, instead of bringing her back to the hospital as he had promised, called a local physician who made a lumbar puncture; she promptly died. There can be no doubt that there was a ventricular tumor, perhaps in the fourth ventricle. You will recall in this connection also the case of colloid cyst of the third ventricle (p. 354).

The second patient (CASE L) was a workman of thirty-three years at the time of admission to the hospital. He had always been strong and healthy until 1929. He had worked hard and saved his money with the idea of marrying and having a family. But in the spring of 1929 his brother induced him to lend his money to help start a restaurant. This failed and all the money was lost. The patient was out of work at the time and stayed in his room brooding over his misfortunes. Then he began to have headaches. At first they occurred a month or so apart but gradually became more frequent. They were thought to be due to worry, but finally became so severe that he was placed in a hospital. Here the physicians could find no cause for his headaches but called them migrainous and gave him some "shots in the arm" which did not help him. Then he tried to work but the headaches were so frequent and severe that he could not do so. For the last six months the headache was almost constant and he vomited frequently without warning. His friends were convinced that the headaches were real although physicians had failed to find any cause for them.

When admitted to the clinic on March 23, 1931, he was very weak and emaciated, holding his head and groaning with pain. It was very difficult to attract his attention and he understood the English language very imperfectly. He was seen to vomit in typical projectile fashion. We were, therefore, very much surprised to find that his pulse rate was 80 and that his fundi were perfectly normal. There was not the slightest trace of papilledema, past or present, and no atrophy of the optic nerves. The visual acuity seemed to be about normal and grossly the visual fields were normal. We were never sure of his coöperation in attempts to determine the visual fields more accurately. The patient maintained he had never had any trouble with his eyes. He insisted that his headaches were always in the frontal region. General physical examination was entirely normal. And the only objective evidence of a lesion of the nervous system that could be found was a

nystagmus on looking to the right and left, coarser and slower on looking to the left. There was no cervical tenderness or rigidity. There was no asynergia, or dysmetria of any of the extremities. He reeled when walking but seemingly from weakness; there was no constant direction of deviation.

In the hospital he slept soundly all night long but as soon as he was awakened began groaning and moaning and holding his head. Roentgenograms of the head were normal. The pineal body was not calcified. There was a normal caloric response from each ear. A lumbar puncture was attempted on three occasions but only a few drops of fluid were obtained. A cisternal puncture was then made. The fluid was under only 30 to 40 mm. of pressure. The pressure rose only very slightly after compression of the jugular veins. The fluid contained 130 lymphocytes per cu. mm. Wassermann reaction was negative on spinal fluid and blood. Complement-fixation test was also negative for echinococcus. The gold-curve was normal. It seemed as though there must be some sort of chronic meningoencephalitis, possibly some rare infection such as with torula, but it was determined to make a ventriculogram to rule out tumor. This was made on April 4. The left occipital horn was reached at a depth of 5 cm. About 20 ccm. of fluid escaped under no tension. The right occipital horn was not found and the needle seemed to pass through a resistance such as a tumor might offer. Roentgenogram showed the air to be confined to the left ventricle which appeared normal. Some air had accumulated in the subarachnoid space along the falx cerebri and this showed that in its posterior portion the lower border of the falx was displaced to the left nearly half a centimeter.

It was planned to make an osteoplastic exploration in the right parietal region but he was already developing a pneumonia from which he died. At necropsy, besides a lobar pneumonia, a most unexpected and unusual condition was found. There is a meningeal tumor 3.5 cm. in diameter indenting the outer upper surface of the right occipital lobe. There is only very slight dilation of the cerebral ventricles. Most striking is a herniation of the cerebral tissue through the incisura tentorii into the subtentorial cavity (Fig. 141). We are familiar with the much more common herniation of the cerebellar tonsils through the foramen magnum and the pain in the back of the neck which results. It may be that the pressure on the incisura tentorii in this case was responsible for the severe headaches without internal hydrocepha-

lus or increased intracranial tension. I have remarked at operation under local anesthesia that manipulation of the incisura causes the patient to complain of severe pain in the forehead because the tentorium is innervated by a recurrent branch of the ophthalmic nerve (354). The specimen demonstrates how rigid the dural septa are (341). The impression of the lower edge of the falx cerebri is clearly visible all along the inner surface of the right cerebral hemisphere.

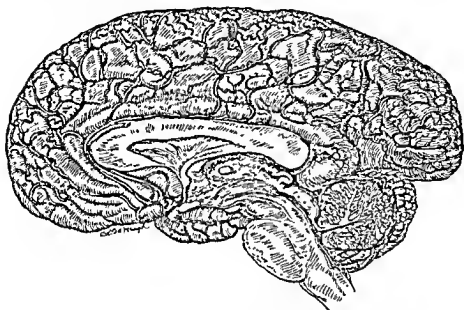


FIG. 141. Brain of CASE L showing herniation of inner surface of right limbic lobe through the incisura tentorii.

This case brings up the question also of *pleocytosis in the spinal fluid* in cases of intracranial tumor. Ordinarily the number of cells is not increased and the content of protein is normal. But in some cases a considerable number of lymphocytes may be present, and especially in cases of tumor around the optic chiasm, for reasons not yet explained; slight changes in the protein-content are often helpful, and gliomas impinging on the ventricular walls sometimes increase the content of protein in the fluid to such an extent that it is definitely yellow in color (214). Perhaps the examination of the spinal fluid might be of assistance in other ways (202), in many instances, but the danger of respiratory failure following lumbar puncture, when the intracranial tension is elevated, is sufficiently great to preclude its use except when

there is some positive indication for such examination.

But to return to our primary interest, the records of these patients I believe will convince you that recurrent bouts of headache should not be lightly classified as migrainous, but should be taken seriously and investigated thoroughly, remembering that they may be produced by intracranial tumor or other serious lesion. We will turn now to another series of patients. You will in your practice become familiar with the middle-aged or elderly patient who begins to complain of headache and to have REPEATED SMALL CEREBRAL INSULTS in which he may or may not lose consciousness but remains afterward enfeebled in various ways. He is usually suffering from sclerosis of the cerebral arteries, one of the frequent lesions which senility brings to the brain.

The brain grows old in many ways. There is what might be called the normal senescence associated with such symptoms as loss of the creative faculty, difficulty in admitting and assimilating new ideas, progressive diminution of memory for recent events, enfeeblement of the will, and blunting of sentimentality. These symptoms accompany such physical signs as diminution of physical force, rapidity of fatigue, slowness and uncertainty of movement, and diminution of general activity. The most common mental change is known as senile dementia (316). Such patients lose their memory for recent events; judgment, reason, and autocratic are enfeebled; they are credulous and suspicious; moral restraints are loosened and sexual instincts are uninhibited. Somatic symptoms are not greater than the age of the patient would indicate. This condition results from degenerative atrophic changes in the cortical neurones, the bloodvessels being little altered. Sometimes a special variety is encountered known as presbyphthia in which judgment and psychic activity are relatively conserved, but there are profound troubles of attention, of memory, and of temporal and spatial orientation, complicated by fabulation and false recognition. Senile dementia is not often confused with brain-tumor. The age of the patient in itself predisposes one to the correct diagnosis and cerebral tumors in advanced age are not common. But such parenchymatous atrophies may occur in younger persons and in these cases confusion with primary cerebral tumors, especially of the frontal lobes, may occur.

This *mān* (CASE LI) of forty years was sent to me suspected of having a frontal tumor. He was quite well until three months before admission to the hospital when he began to feel uncomfortable in a vague general way without any definite symptoms. He became tired and sleepy. At

first he was able to go to his office and continue his work but later he stayed at home. He could be aroused at meal-times to eat but slept almost constantly otherwise. His memory rapidly failed. He lost all interest in his business or sports and had increasing difficulty in the use of the right arm and leg. He stumbled often in walking and dragged the right leg.

When admitted to the hospital a month ago he was very lethargic and slept most of the time. His memory was obviously very defective; his speech was slurred and slow. There was diplopia on looking to either side. The left pupil reacted normally; there had been an old injury to the right one. He had a right lower facial weakness and a right hemiparesis with slightly increased reflexes. The right abdominal and cremasteric reflexes were absent but no sensory loss could be detected. There was no ataxia and he walked with a slightly hemiplegic gait. General examination of the viscera was normal. His bloodpressure was 130/90. His basal metabolic rate was -27 ; but he slept throughout the test. Wassermann reactions on the blood and spinal fluid were negative. Examination of the blood and urine was normal. During his stay in the hospital his temperature ranged from 36° to 37.4° . His pulse-rate varied from 60 to 85. There was no choking of the optic discs. The diplopia seemed to be due to a bilateral weakness of the internal rectus muscles. It seemed evident that there was a lesion of the left frontal lobe, but the nature of it was not certain. An infiltrating glioma was thought to be the most probable diagnosis since there seemed to be no evidence of lues or of arteriosclerosis and no primary tumor was found from which metastases could have occurred. The sleepiness made one think of an encephalitis but there seemed to be no other evidence of inflammation of the brain, and this might be explained by invasion or distortion of the hypothalamus by a tumor. Operation was advised but his relatives decided to seek other advice.

He was taken to another hospital where the same diagnosis was made and returned here a week later. In the meantime he had become obviously worse. He was now unable to walk, and difficult to arouse most of the time. But when awake he was very turbulent. The nurses had great difficulty in keeping him in bed. He insisted that he had to get up and attend to his business. The right facial weakness was much more obvious and the right hemiparesis was also much more pronounced. In spite of the absence of symptoms of intracranial tension the

rapid progression of symptoms made us feel fairly certain that we were dealing with an infiltrating glioma, probably of the corpus callosum, extending into the left frontal lobe. A roentgenogram of the head showed that the pineal body was exactly in the midline. There was at this time evident loss of sensation to pain on the right side of the body. He would not coöperate for an accurate sensory examination. There seemed to be no defect in the visual fields although his coöperation left much to be desired. It was determined to explore the left frontal lobe, and this was done under ether-anesthesia.

The dura mater was found to be quite tense but as soon as it was opened a great amount of fluid came out, reducing the tension. The brain was very atrophic and injected. There was a great excess of subarachnoid fluid and the veins were all covered with a whitish exudate. No softenings were observed. A fragment of frontal convolution was removed for examination and the wound carefully closed after control of the bleeding. The patient reacted very badly after the operation. His temperature rose to 40.2° and his pulse rate to 180. The temperature was kept down by sponges with alcohol and packing with ice but two days later, when the sponging was stopped, it again went up to 40° . He did not entirely regain the ability to regulate his temperature until the eighth day after operation and it has remained slightly elevated ever since. During the early postoperative days he was completely comatose, very restless, breathing stertorously, and very cyanotic. He has now recovered consciousness, but still breathes rapidly and is quite disoriented. Microscopical examination of the cortex removed showed the changes in the cortical neurones typical of Alzheimer's disease. No softenings were present and the cortical bloodvessels were normal. The man's brain, then, had grown old before its time, and the cortical cells had failed before the bloodvessels.

Presenile dementia is not frequent. Different varieties have been described but all are characterized by premature and rapid failure of the mental faculties, disorientation and confusion, a tendency to turbulence and violence, stereotyped repetition of speech and gestures, and negativism. In all of them are found cortical atrophies, either general or circumscribed, with relatively intact bloodvessels in the brain. It is impossible in our case to explain in detail the symptomatology without the entire brain to examine. The rapid development of focal symptomatology is at any rate unusual. Focal symptoms are found in the so-

called Pick's atrophy but in this disease the intraneuronal changes of senile atrophy are absent.

Much more frequently the bloodvessels of the brain become degenerated before the neurones, which are only secondarily involved by ischemia. The symptoms are produced by the death of neurones as their bloodsupply is shut off by gradual or sudden occlusion of the sclerotic vessels. The symptoms, therefore, develop frequently in successive episodes which vary from slight dizziness to attacks of apoplectic coma. The symptoms are quite varied, depending on the location of the diseased vessel, and depending also on the completeness of the occlusion, and the size of the vessel. Besides sudden hemiplegia and other major accidents one observes a long series of vertigoes, spasms, transient palsies, and epilepsies. Mental symptoms are also produced by arteriosclerosis but are more focal in character than those observed in senile dementia and evolve also in attacks. One of the earliest symptoms is difficulty in fixing the attention and rapid fatigue by any intellectual activity. It is rare to see in these cases the profound mental poverty associated with the primary cortical atrophies; there seems always to be a nucleus of the personality conserved, which serves to distinguish these patients from those suffering from general paralysis or senile dementia. However, attacks of apathy, stupor, confusion, or agitation may be tenacious.

If we recall how one of the earliest signs of a glioblastoma multiforme may be an inability to concentrate on one's intellectual activity, accompanied by attacks of vertigo and fainting (cf. case XXXIII), we begin at once to appreciate the difficulty of differentiation. When we remember also that choking of the optic discs in these tumors may be absent for a long time or completely, the difficulty becomes still more apparent. It is increased by the fact that headache is an almost constant accompaniment of cerebral arteriosclerosis and that choked discs are not uncommon (3). It is useless to depend upon general arteriosclerosis to aid in the differentiation because cerebral arteriosclerosis may exist with no discoverable sclerosis of the rest of the vascular system. Of course there are symptoms more or less characteristic of the cerebral arteriosclerosis which aid in detecting certain cases. Such are the troubles of gait. These patients walk with short steps, dragging the feet on the floor. The movements of the upper extremities also are feeble and awkward. These patients speak with a monotonous voice, articulating poorly; the lower face is weak and they may drool saliva. The inactivity of the

lower face contrasts markedly with the animated expression of the eyes. They have spasmodic laughing and crying. Their movements are slow and stiff, with loss of automatism. All of these symptoms result from repeated small lesions in the deeper regions of the brain and rarely are marked in cases of cerebral tumor. Pseudobulbar palsies are also rare with brain-tumor. But in many arteriosclerotic patients these symptoms are also absent. When any middle-aged or elderly patient begins to suffer from repeated episodes such as we have mentioned, the possibility of cerebral neoplasm must be thought of along with *cerebral arteriosclerosis* and *lues*. That the differentiation in the early stages of the disease may be difficult we can appreciate from the study of such a case.

The patient is a married woman of forty years (CASE LII) previously well until a year ago. While using the telephone she suddenly became speechless, her vision blurred and dimmed. She did not lose consciousness and had no paralysis of her extremities. A physician was called who said she had heart-disease and softening of the brain. Her speech returned after about an hour. She was kept in bed for three weeks. During this time she had two exactly similar attacks, one when she had risen to go to the bathroom. She then became melancholy and cried a great deal, whereas formerly she had been of a cheerful disposition. She later began to have spasms in the right side of the face, several times a day, and lasting for only a few minutes. She continued to be depressed and to have the twichings in the face. There was no more difficulty with speech. Two months later she improved, was entirely free from symptoms and thought she was well, but soon the twichings of the face began again and continued for a couple of months. She then felt perfectly well and went to visit in another city. Here she suddenly had a violent headache, the right arm became weak and awkward, and her speech became slow and indistinct. The headache gradually disappeared. There had been no vomiting.

When admitted to this hospital a month ago she was somewhat apathetic and depressed. Her speech was slow and slurred. She understood spoken and written language fairly well, but in speaking spontaneously many words were recalled with difficulty. There was no choking of the optic discs; the fundi and visual fields were normal. There was a paresis of the lower right side of the face. The right upper extremity was weak, particularly distally. The right wrist and biceps-jerks were brisker than the left. There was a coarse action-tremor of both hands,

especially of the right. The abdominal reflexes were absent. The right lower extremity was weak, especially the flexor muscles. The right knee and ankle-jerks were slightly exaggerated but there was no clonus and no extensor plantar reflex. Two-point discrimination was poor in the right hand and stereognosis seemed somewhat deficient. The pulse rate ranged from 78 to 104. The temperature ranged from 36.2° to 37.6° . The internal organs seemed normal, the heart particularly. Roentgenogram of the head was normal except for a small calcified area in the dura mater over the left frontal lobe; the pineal body was not visible. The examination indicated a lesion of the lower central region of the left cerebral hemisphere but its nature was not clear. The history was that of an intermittent vascular spasm with final occlusion, but no evidence of cardiovascular or renal disease was present except that the systolic bloodpressure was 188. It was decided to explore the region.

An osteoplastic operation disclosed a grayish-red discoloration of the anterior and posterior central convolutions about 2 cm. above the lateral fissure. This area was firmer than the cerebrum anteriorly. The region of the supramarginal gyrus on the contrary was flattened, yellowish, soft, and avascular. A fragment of the posterior central gyrus was removed for examination and the wound closed, after making a decompression over the subtemporal region. The brain was not at all tense. She had a postoperative hemiplegia and an aphasia, both of which slowly improved. Examination of the tissue removed showed the lesion to be a glioblastoma multiforme, so roentgen-radiation was begun. Today, a month after operation, you see that she is much better. She obeys simple commands and points out ordinary objects by their names. Her speech, however, is confined almost exclusively to "yes" and "no." The decompressed area is bulging very slightly and is soft. The right leg is spastic but she can walk. The right arm is almost totally paralyzed and the right lower face also.

There was in this patient an infiltrating tumor which had not increased the intracranial tension, and in addition a softening doubtless caused by occlusion of a branch of the middle cerebral artery by the tumor. *This combination of glioma and softening is not infrequent (407).*

Among the symptoms produced by arteriosclerosis of the brain we mentioned *epilepsy*. It is also produced by lues and by cerebral tumors (495). Again when a middle-aged or elderly patient develops epilepsy for the first time these three possibilities must be kept in mind. An

EPILEPTIC ATTACK is a symptom, as is headache or dizziness, but such attacks characterized by recurrent loss of consciousness, with or without convulsions, occur in persons who have no physical signs of disease. This condition is known as idiopathic epilepsy.

Because no constant structural lesions have been demonstrated in the brains of these idiopathic epileptic patients a constitutional element has been postulated and this element, the nature of which is unknown, is said to be hereditary. At least in the general population only 5 or 6 percent have epileptic ancestry whereas a family-history of epilepsy can be obtained in some 30 percent of epileptics. The reason why the inherited predisposition cannot be figured according to the laws of heredity is probably that the predisposition can be tested only by injury to the brain. Some lesion to the brain seems to be necessary to act as a trigger for setting off the attacks. Even in the so-called idiopathic cases there is probably a diffuse cerebral damage which has resulted from intra-uterine conditions, infections in infancy, or injury at birth. The last mentioned cause is probably very important. It is reckoned that 34 percent of children dying from birth-injury are first-born and 27 percent of epileptics are first-born children (74). There is another evidence of the hereditary tendency in the frequency of infantile convulsions, which are five times as common in the children of epileptics as they are in those of normal parents. Early convulsions occur in more than 20 percent of idiopathic epileptics and in less than 4 percent of normal individuals (371).

The condition of idiopathic epilepsy develops in over 50 percent of cases before the age of fifteen, in over 85 percent before the age of thirty, and in over 90 percent before the age of forty. This means, of course, that whenever a previously normal individual develops epileptic attacks in middle life the latent predisposition has usually been revealed by a fresh lesion in the brain and its nature must be carefully sought. Aside from external violence the three most common causes are arteriosclerosis, syphilis, and cerebral neoplasm.

This shoemaker (CASE LIII) of forty-eight years had always been well until seven months ago. While at work he lost consciousness and was told afterward that he had a generalized convulsion. About two months later he began a series of convulsions and soon lapsed into a stupor from which he slowly recovered. He was then taken to another clinic where nothing definite was found. He was told that he had epilepsy of unknown origin and advised to return in a few months for fur-

ther examination. There were no more convulsions but he continued to grow weak and gradually developed a numbness of the right hand. About two months ago he began vomiting, complained for the first time of headache, and was admitted to this clinic.

He was then very weak and emaciated. There was a left lower facial weakness, the left knee-jerk was brisker than the right but there was no extensor plantar reflex. He comprehended slowly, easily lost the thread of conversation, and was disoriented in the ward so that he could not find his own bed. There was also some tendency to perseveration of motion in the left hand, with at times forced grasping. The optic discs were choked and elevated about two diopters, with numerous small hemorrhages over the discs. An attempt to examine the visual fields failed because of inability of the patient to coöperate. Grossly he seemed to have a left hemianopia. The ocular movements were synchronous but not full, rather slow and jerky. There seemed to be definite weakness of the anterior flexors of the head and these muscles were atrophic and flabby. There seemed to be definite atrophy of all the muscles of the right shoulder-girdle, subsequent to a fall from a ladder some years previously; movements of this shoulder were normal. He walked with short steps and occasionally swayed backward. His pulse rate varied from 75 to 100; temperature was definitely subnormal, ranging every day from 35.5° to 37°. Because of the unusual number of hemorrhages in the retina with only a low choking the ophthalmologist diagnosed hemorrhagic neuroretinitis. I felt that the patient probably had a tumor, no cause being found for a neuroretinitis. There was no evidence of lues or of cardio-renal disease. But the localizing symptoms were not very clear. I rather favored the corpus callosum as a possible location with an extension into the right frontal lobe. A ventricular puncture was attempted. An opening was made in the right occipitoparietal region and a needle directed toward the lateral ventricle entered a cystic cavity at a depth of three centimeters from which yellow clotting fluid was obtained. An osteoplastic operation then disclosed in the right temporo-occipital region the superficial extension of a reddish-gray glioblastoma multiforme. A considerable portion of it was removed. His mental condition has now improved and it is possible to prove that he has a left homonymous hemianopia.

When this man was examined in the first clinic his condition was impossible to diagnose. There is a great tendency for the specialist who sees these patients in the last stages of their illnesses to be impatient with

the general practitioner and to think that the diagnosis of brain-tumor is simple. Neurologists are not immune to this failing and neurosurgeons seem peculiarly prone to it. A few years in general practice or even in a general neurological clinic would exert a very salutary influence on such persons. In these doubtful cases I would insist only that the practitioner keep in mind the possibility of brain-tumor more often than he seems to, probably from lack of appreciation of its frequency.

In the preceding case, although it was impossible to determine the cause of the epileptic attacks at the time of his first examination, idiopathic epilepsy was not considered because of the age of the patient and the rapid development of paralytic phenomena but I should like to tell you of another patient in whom convulsions began earlier and continued for years, who was treated by a number of competent neurologists as an idiopathic epileptic, yet finally died of an intracranial neoplasm.

This young woman (CASE LIV) at the age of twenty-three had a generalized convulsion. Previously she had been well and no history of injury at birth, infantile convulsions, or other suggestive factor could be obtained. Similar attacks recurred at intervals for a year. The following year she had fainting-spells and the third year no attacks under treatment by competent neurologists for idiopathic epilepsy. She then continued to have minor attacks until the age of twenty-nine, when she began to have peculiar ideas, and to be unable to concentrate on her work as a school-teacher. At that time her attacks consisted of a change in color, an occasional grunt, and a weakness in the legs, with an occasional momentary loss of consciousness. She usually felt that something was coming on and had time to sit down. She was having these minor attacks almost daily in spite of large doses of luminal and bromides. After two years passed in this way she had a spell during which she was sleepy, disoriented, and indifferent. The following year she became very lethargic. During all this time repeated examinations by different neurologists could disclose no evidence of involvement of the brain apart from the attacks. Finally at the age of thirty-three for the first time she began to complain of headache and her attacks changed. They then began in the right hand which always moved toward the face by flexion of the right forearm. After an attack the right arm was limp and weak. A right facial weakness developed but there was still no choking of the optic discs. She became mentally quite dull. During the subsequent six months she suffered from violent headaches with vomiting. She began to "shuffle" her feet in walking and finally became bedridden. She developed an

unusual thirst and passed large quantities of urine. She seemed not to understand when spoken to. She finally became comatose and was brought to a hospital where she died within a few hours. Her pulse rate was around 60; she was vomiting and stuporous. A neurological examination was not made but a roentgenogram showed the dorsum sellae to be absent. Although there was no necropsy there can be no doubt that this patient was suffering from an intracranial neoplasm in the region of the third ventricle. The first suspicion that such a lesion might be present arose ten years after the onset of her trouble.

These patients teach us that we must look upon epilepsy as a symptom and be constantly on the lookout for the precipitating lesion in the brain. Finally I should like to point out that the epileptic seizures which are caused by tumor are not always of focal character. It is remarkable that a patient who is developing a brain-tumor may have, without any premonitory symptoms whatever, a violent generalized convulsion with loss of consciousness which is followed only many weeks, months, or even years afterward by focal attacks and finally symptoms of increased intracranial tension. Such generalized convulsions of course have no localizing significance.

Until now we have spoken chiefly of adults but there is one symptom in childhood which is particularly suspicious, and that is RECURRENT VOMITING. Vomiting may be the earliest and for many weeks the only symptom of intracranial tumor in children. Of course children vomit easily and for a multitude of reasons, but persistent recurring vomiting should be taken seriously. We are not here concerned with the vomiting of early infancy, because infants rarely have intracranial tumors and when they do have them the earliest, and often for a long time, the only symptom is enlargement of the head.

The most common repeated vomiting of childhood is the so-called cyclic vomiting (415). It occurs in nervous children, beginning between three and six years of age and continuing intermittently until puberty. At intervals of weeks, months or years these children have attacks of vomiting. In a typical seizure the child is irritable and restless, complains of thirst and of indefinite pain in the stomach. He may be sleepy and lethargic. He has a distressed expression on his face. Most important however, is the fact that he vomits so persistently that he is unable to retain either solid or liquid food; so he loses weight rapidly. He rapidly develops ketonemia. Ketone-bodies are excreted in the urine and breath and the odor in the room is characteristic. There is often at the same

time a hypoglycemia. There is perhaps also lipemia; the enlargement of the liver is usually attributed to fatty infiltration of this organ. After a time the vomiting ceases, the child rapidly gains in weight and is apparently none the worse for the episode. The cause is not known.

The typical case of cyclic vomiting should cause no difficulty in diagnosis, and most cases of intracranial tumor in children are readily diagnosed. A child who has vomited may be fed immediately afterward and retain his food perfectly. The vomiting of tumor is often forceful and unaccompanied by abdominal distress, yet this is not always so and there may be intense nausea. I have seen two children with cerebellar tumors who vomited so constantly and with such abdominal distress that they were treated for weeks by well-trained pediatricians for cyclic vomiting. I will show you a child with persistent vomiting and you will see that it is not always so easy to determine the cause.

This is a male child (CASE LV) of twelve years who was perfectly well, except for the usual children's diseases, until two months ago when he came home from a picnic and began vomiting. Since then he has been unable to retain any food. There have been no other symptoms, no temperature, no pain or headache, no nausea even. He has become much emaciated and very weak.

On admission he was badly dehydrated, with a marked acidosis. Temperature was 37.2° per rectum. The acidosis was combated by intravenous glucose (10 percent) and hypodermoclyses of normal saline solution but the vomiting persisted. No adequate cause could be found for the vomiting. Roentgenogram of the head was normal. There was no choking of the optic discs. A barium-meal disclosed no organic lesion of the esophagus, stomach, duodenal bulb, or intestine. An intracranial origin was suspected but careful neurological examination revealed only coarse inconstant nystagmoid movements of the eyes when looking laterally. The boy was generally hypotonic, and the tendon-reflexes difficult to elicit; some unsteadiness of the extremities was evident but these findings were of doubtful significance in view of the extreme weakness and emaciation. There was no stiffness or tenderness of the neck nor had there ever been any pain in the neck or headache. Once it was thought that the tendon-reflexes on the right side were slightly brisker; another observer noted that the right knee-jerk was especially difficult to obtain. There was no difficulty in swallowing. In spite of the meagerness of the symptoms an exploration was advised on the possibility that there might be a tumor in the fourth ventricle.

A midline incision was made under local anesthesia. In the floor of the fourth ventricle was found a solid yellowish mass 1.5 cm. in diameter, bulging from the bulb itself into which it spread without sharp transition. It was obviously a tumor of the bulb and its extirpation was judged impossible. I was even afraid to attempt to remove a fragment for determination of its histological nature. That evening the child's temperature rose to 40° but subsided promptly. He still vomits repeatedly but on the whole now, eleven days after the operation, he is able to retain some food and is gaining strength. We may remember in this connection also the young lad with the suprasellar cyst, who suffered from repeated attacks of vomiting and epigastric distress from an early age (p. 113).

Finally, I should like to discuss briefly FAILURE OF VISION as a symptom of intracranial tumor. I have no doubt that if a patient came to almost any physician complaining of the triad of headache, vomiting and failing vision, the physician would think of an intracranial tumor as a possible cause, but failing vision without the other two symptoms seems not to suggest this diagnosis as readily as it should.

Consider the plight of this young man (CASE LVI) of twenty-four who applied for a job as a taxi-driver four years ago. He was told that his eyes were not good enough, and consulted an ophthalmologist who gave him glasses. They did not help his vision so a few months later he went to see another ophthalmologist who told him that the right retina was "abnormal from birth" and changed his glasses. The next year he was told by a physician that he had glandular trouble and was given thyroid, testicular and pituitary extract. This seemed to make him feel better for a time but did not help his vision. He then trailed from one physician to another. Six months ago his vision became much worse but it was not until a month ago that a physician for the first time told him that there was a tumor pressing on his optic nerves and advised an operation for relief.

I think none of you would now have any trouble in making the correct diagnosis. His body has an infantile rounded appearance and is practically hairless. The skin is pale, pasty, and finely wrinkled, especially over the face. There is no beard. The genitalia are quite small. He is sluggish and sleepy. He has a primary optic atrophy in each eye. The right eye can see only gross movements. The left eye has a temporal hemianopia, but the vision is 1.0—3. His basal metabolism is about —30. Roentgenogram of the head shows the sella turcica to be marked-

ly enlarged, ballooned from within. It is the typical picture of a chromophobe adenoma of the hypophysis.

Further inquiry reveals that he began to have erections and nocturnal emissions at fourteen and to shave at fifteen years of age. But he never had a heavy beard and shaved only once a month. He thinks that his axillary hair began to disappear four years ago. He never had much hair over the body. Two years ago he ceased to have nocturnal emissions. He thinks also that his genitalia have decreased in size in the last two years and he has now no sexual appetite at all. In the past two years also he has become very tired and sluggish. There has never been any polyuria or polydipsia. It seems incredible that such a patient could pass through the hands of numerous physicians in the course of four years while he developed all of the classical symptoms of this condition and that his eyes should have been examined repeatedly by ophthalmologists (not oculists) without the obvious changes being correctly interpreted. Yet this is exactly what happened.

The young physician should acquire an ophthalmoscope as early as a stethoscope and learn to use it as well (467). He will see many things with it that he cannot interpret but he can at least learn to know the normal fundus and detect variations from normal. He will find OPHTHALMOSCOPY distinctly useful as an aid in the diagnosis of many obscure cases. With a little experience he can learn to detect the pathological alterations important in the diagnosis of intracranial tumors, namely optic atrophy, both primary and secondary, and papilledema. The optic nerve-head may be swollen either from actual inflammation or from stasis of its drainage along the optic sheaths. It is necessary to distinguish, therefore, between optic neuritis and papilledema which in its exaggerated form is known as "choked disc."

In optic neuritis the papilla is abnormally reddened and clouded. Its boundaries are obscured and slightly elevated. The retinal arteries are little affected but the veins are widened and tortuous. There is always a peripapillary edema but seldom hemorrhages in the retina. There are often central scotomas and it is characteristic that the visual acuity is very much diminished, out of all proportion to the damage visible with the ophthalmoscope. An early papilledema differs from this picture. The papilla is again reddened but not diffusely so; many dilated capillaries are visible over the disc. The boundaries are obscured and slightly elevated. The veins are engorged; the arteries are little affected but tend to curl over the margin of the disc. The physiological cup is filled, but most

important is the fact that there are no scotomas and the visual acuity is usually normal.

When the *papilledema* reaches such an intensity that the disc is elevated more than two diopters there is said to be "choking" of the disc (Fig. 142). The swelling may reach seven or eight diopters. The arteries are small and hidden over the disc by the edema; the veins are engorged and very tortuous. The edema extends out into the retina, so that it is impossible to determine the exact margins of the disc which appears much enlarged. Over the disc are numerous small engorged capillaries. Hemorrhages begin over the disc and are found even far out in the

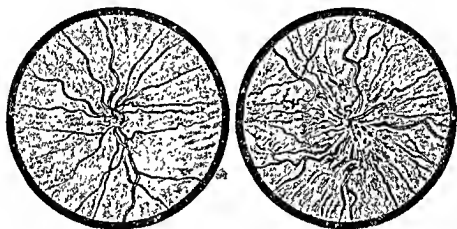


Fig. 142. Fundi oculi. At the left, an early choking; at the right, advanced choking.

retina. It is remarkable that vision may remain fairly intact for a long time after the swelling has become intense. The visual fields are first generally constricted and the blindspots enlarged. Then come transient periods of darkening of vision and finally, often quite suddenly, vision is lost. After vision is lost, if not before, secondary atrophy sets in. The swelling of the papilla subsides; the hemorrhages are absorbed or organized into whitish scars. The veins return to normal caliber. The optic nerve becomes white, but its margins are not sharply outlined.

A choked disc may be produced by a purely mechanical obstruction, as from tumor, whereas an optic neuritis is caused by an actual inflammation. The latter, however, also causes edema of the nerve-head even though it rarely rises over two diopters. There are many causes of optic

neuritis and many of them may produce changes in the retina difficult to distinguish from those in a pure choking. In luetic neuritis the papilla is red and much enlarged, with a gray ring of edema around it. The veins are engorged and white lines accompany them over the disc. The recognition of this type is often aided by patches of old choroiditis with atrophy and abnormal pigmentation. There may also be slight clouding of the vitreous humor. Tuberculous neuritis can be distinguished only by finding tubercles in the retina. It may be suspected in children who have active tuberculosis elsewhere. Nephritic, so-called albuminuric, neuritis is distinguished usually by extensive hemorrhagic and degenerative changes throughout the retina, but in some cases in which the lesions lie around the optic disc the picture may resemble closely a choked disc. Arteriosclerotic neuritis is distinguished by its chronic course. There are white lines along the bloodvessels and the veins are constricted where the arteries cross them. The edema of the papilla is usually slight but can also be intense enough to simulate a choking.

The greatest difficulties arise in the nephritic-hypertensive-arteriosclerotic group (66). These degenerative affections have approximately the same age-range as the most common and malignant intracranial tumor, the glioblastoma multiforme. We have already learned how difficult it may be to differentiate these conditions by the symptoms. It would be a great help if the ophthalmoscope could more definitely settle this diagnostic problem, but often the ophthalmoscopic findings are as equivocal as the neurological symptoms. The findings of nephritis, vascular hypertension, or general arteriosclerosis can be used only as one factor in the diagnosis because a nephritic, hypertensive, or arteriosclerotic patient may develop a cerebral tumor and often does so. In uncomplicated arteriosclerosis the nerve-head is reddened; there is rarely any edema; the arteries are contracted, beaded, with whitish sheaths and plaques along their walls; they compress the veins where they cross them. The light-reflex of the arteries is increased. There is apt to be extreme tortuosity and increase in the number of the arterial branches in the region of the macula. Hemorrhages in the nerve-fiber layer and whitish ischemic spots in the retina are common. In hypertension the arteries are smooth and round, but elongated and tortuous. The reflex stripe is increased and the arteries constrict the veins where they cross them. The arteries are not sheathed or beaded. There is often edema which may elevate the papilla several diopters. Again small isolated or grouped plaques and hemorrhages in the peripheral retina

are common. In the cardiovascular-renal disease of middle-aged or elderly persons, nephritic, arteriosclerotic, and hypertensive changes are often combined and are usually to be distinguished from those of "choking" by the more extensive lesions in the peripheral parts of the retina and by the lesser degree of edema of the papilla.

The *primary optic atrophy* produced by direct pressure of a tumor on the optic nerves or tracts is usually indistinguishable ophthalmoscopically from that due to other causes. The nerve-head in the final stage is very white and sharply outlined, the border being often pigmented (Fig.

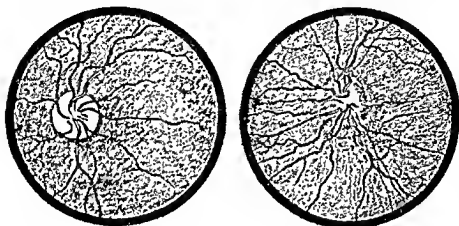


Fig. 143. Fundi oculi. At the left, a primary optic atrophy; at the right, atrophy following choked disc.

143). The central part of the disc is usually mottled with gray, especially toward the temporal side. The bloodvessels are small and distinct. As the atrophy develops the paling of the disc is evident earlier on the temporal half. Primary optic atrophy from tumor must be distinguished especially from that caused by syphilis. The differentiation is made from accessory data. In lues the pupils are irregular and react imperfectly to light; all the other symptoms of neurosyphilis are taken into account, the appearance of the disc itself not being pathognomonic. The *post-neuritic* or *postedematous atrophy* is characterized essentially by the obscured margins of the disc and the absence of mottling (Fig. 143).

The appearance of the optic disc in an early atrophy caused by pressure of a tumor on the optic nerve is not different from that caused by degeneration of the macular bundle in a retrobulbar neuritis. In each case the temporal half of the disc is pale, the only change to be seen

with the ophthalmoscope. Yet it is important to differentiate the two conditions, because retrobulbar neuritis is rarely caused by intracranial tumor. The differentiation is made by examination of the visual fields. Pressure on the optic nerve usually causes peripheral defects of the visual fields whereas retrobulbar neuritis causes typically a degeneration of the macular bundle and hence central scotoma. The presence of central scotomas and normal peripheral fields should make one search for evidences of multiple sclerosis, intoxications, or sinus-disease, although such defects may be produced by craniopharyngiomas. *Unilateral central scotoma is an early symptom of meningiomas of the olfactory groove.* }

The visual fields are best examined quantitatively in a constant illumination by the use of minute white test-objects (489). For this purpose a screen is better than a perimeter. Defects of the peripheral fields are of such paramount importance in the localization of intracranial tumors that any amount of effort is worth while to determine their presence.

We have noted then as symptoms which should arouse the suspicion of the physician: (1) in infants, enlargement of the head; (2) in children, vomiting; (3) in adult life, repeated cerebral insults, epilepsy, and recurrent headache; and (4) at all ages failing vision. *When confronted with a patient who has symptoms of a progressive lesion of the brain the physician must always make a threefold diagnosis:* (1) the location of the lesion, (2) the nature of the lesion, and (3) if a tumor, its pathological type. We have discussed sufficiently the last diagnosis and have learned in what instances it is possible to make a diagnosis of pathological type and how. We have learned also the symptoms which arise from the development of a tumor in the different parts of the brain; it needs to be emphasized, however, that *these neurological symptoms of localization are often treacherous in cases of brain-tumor.* 1

The neurological symptoms caused by intracranial tumors may be divided theoretically into (1) focal, (2) neighborhood, and (3) distant. The area in which the tumor originates is irritated or destroyed and gives rise to the earliest symptoms. As the growth increases in size it invades neighboring regions, presses on others or causes edema in them and thus produces neighborhood-symptoms. Symptoms from regions distant from the lesion are produced in several ways, usually as a result of increased intracranial pressure, but sometimes by occlusion of large arterial or venous trunks, by blockage of circulation of cerebrospinal fluid, or by edema. The symptoms thus have a tendency to

develop in the order of local, neighborhood, and distant symptoms. For this reason it is very important in taking the history to *establish the chronological order of development of the symptoms*. But it should be remembered that this order is not always followed. A glioma of the tip of the temporal pole may cause first distant symptoms by occlusion of the middle cerebral artery and then neighborhood-symptoms by pressure on the uncus, whereas the local symptoms are never detected because no symptoms as yet demonstrable are produced by lesions of this region of the brain, at least of the right hemisphere.

There are large areas in the brain where lesions may reach a considerable size without producing symptoms noticeable to the patient. These are the frontal lobes, the right posterior parietal region and the occipital lobes, the right temporal lobe and the tip of the left temporal lobe. Careful examination in these cases will usually reveal a defect—an alteration of character, defective memory, astereognosis, or a defect in the visual fields, but the fact remains that many of these patients complain first of neighborhood-symptoms; the patients with tumors of the frontal lobe may complain first of epileptic attacks, those with tumors of the occipital lobe of difficulty in reading, those with tumors of the temporal lobe of hemiparesis. And there are even cases in which the most detailed questioning and examination will reveal only the symptoms and signs of increased intracranial tension.

Some of the distant symptoms have become notorious (106). They may be produced by tumors anywhere in the intracranial cavity and should never be given localizing significance unless they occur early and are supported by much confirmatory evidence. In the presence of high intracranial tension they must always be discounted. Foremost among these false localizing symptoms is paresis of the sixth cranial nerve. This nerve runs for quite a distance on the under surface of the pons and is readily compressed between it and the branches of the basilar artery by anything which increases the tension within the brain. The olfactory nerves are similarly exposed; moreover, nasal affections in our climate are so frequent that great impairment of olfactory function is frequent. Stiffness and pain in the back of the neck, although more frequent with tumors in the cerebellar fossa, may be caused by tumors anywhere in the intracranial cavity when the intracranial tension is high. No emphasis should be placed on the location of the headache or on localized tenderness of the scalp or skull unless supported roentgeno-

logically by alterations of the skull in the same area. Rarely paresis of the third and fifth cranial nerves also may be produced by pressure from a distant tumor. The auditory nerve may be "choked" (168) in much the same way as the optic nerve, causing tinnitus and deafness. Adiposity and genital dystrophy in the child and young adult may be caused by cerebellar tumor (132); in this case the dilatation of the third ventricle from internal hydrocephalus acts in the same way as a primary infundibular tumor. Conversely a suprasellar tumor may cause marked unsteadiness of gait (32). The differential diagnosis of tumors in the third and fourth ventricles is thus rendered peculiarly hazardous. Compression of the cerebral peduncle against the tentorium cerebelli may cause homolateral pyramidal symptoms (298).

To add to the difficulties of localizing an intracranial tumor, the patient's memory may be defective, or he may be aphasic, so that he cannot give his history. From mental disturbance he may be unable to coöperate in an essential examination, such as that of the visual fields. He may even be in coma and no relatives be present to relate the course of the illness. In this situation the physician is compelled to practice what is practically veterinary medicine.

But the physician can aid himself in various ways. If the intracranial tension is high he may begin by injecting intravenously a hypertonic solution (50 ccm. of 50 percent glucose is best). Fluid is thus removed from the brain and subarachnoid spaces into the bloodstream and intracranial tension thereby reduced. The resulting change is sometimes remarkable, especially if there be an internal hydrocephalus. It is rare that some improvement does not occur. The effect however lasts only a few hours at best and is difficult to repeat so that one must make the most of the transient period of improvement.

More lasting improvement may be obtained by removing a portion of the skull by operation, the so-called decompressive procedure. This gives the brain a chance to expand and reduces intracranial tension. Symptoms produced by tension then improve whereas symptoms produced by the local infiltration of the tumor are often accentuated (92). But in interpreting the latter symptoms one must be careful to discount those due to herniation of the brain through the decompressed area. When the opening is made in the temporal region the symptoms sometimes produced by herniation are hemiparesis, most noticeable in the face, and, if the opening be on the left side, aphasia.

But the decompressive operation is now little used for this purpose since the development of the procedure known as VENTRICULOGRAPHY (152). The ventricles of the brain have a known shape and situation within the skull. It is evident that an expanding lesion must distort and displace them (Figs. 144 and 145). The ventricles may be rendered visible by replacing their fluid content with air. Since the air is of less density it is visible in the roentgenogram. When this procedure was discovered many thought that there was no longer any need of a pains-

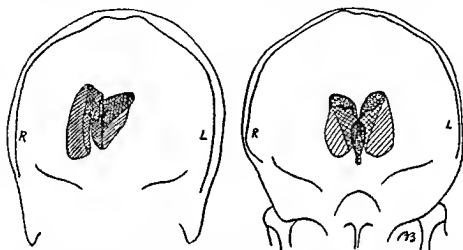


FIG. 144. Scheme of anteroposterior ventriculograms. At the left, the ventricles are distorted and displaced by a large left frontal tumor; at right, the ventricles are in normal position but slightly dilated. Compare Plates X and XI.

taking search for neurological symptoms and signs. A simple injection of air was thought to be sufficient. But experience has taught otherwise. The roentgenograms are often difficult to interpret and the procedure has been found to be not without danger to the patient. *Symptoms are exaggerated and death sometimes results from its use (374).*

It is difficult by the method of ventriculography to obtain a clear image of the third and fourth ventricles. The air either does not enter them or they are so narrow that the shadow cast by the air is not sufficiently dense to be clearly visible. This is a most unfortunate defect of the method because the differentiation between tumors of the third and fourth ventricles is often very difficult to make on the basis of the symptoms. The third and fourth ventricles are more easily filled by the method of encephalography, in which the air is introduced by lumbar puncture,

but this method is dangerous in the presence of increased intracranial tension, especially if the tumor is in the posterior cranial fossa, and hence is seldom used in cases of intracranial tumor. It is also difficult to interpret the shadows of the temporal horns. I have been repeatedly led astray by supposed defects of these portions of the ventricular system. And the occipital horns are normally so variable in size, length, and direction that they must be interpreted with great caution. *Ventriculography should, therefore, be resorted to only when necessary*, in my experience in about fifteen percent of cases, and even then often

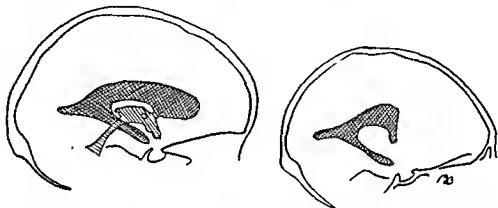


FIG. 145. Scheme of lateral ventriculograms. At the left, the ventricles are dilated but in normal position; at the right, the anterior horn is deformed by a large right frontal tumor which has also occluded the interventricular foramen so that no air has entered the third ventricle. Compare Plates X and XI.

leaves one more puzzled than ever. I have found this method most useful in detecting tumors of the frontal lobes. The frontal horns of the lateral ventricles are fairly constant in size and position, readily filled with air and easily demonstrated in the roentgenogram.

It should not be forgotten also that ventriculography does not make a diagnosis of tumor but only of distortion or displacement of the ventricles. The pathological nature of the disturbance must be determined otherwise. This may sometimes be accomplished by the method of ARTERIOGRAPHY in which a radio-opaque substance is injected into the carotid artery (346). This method gives some hope of being able to detect glioblastomas in a large percentage of cases, because of the abnormal vessels which they contain, and makes the diagnosis of angiomas and aneurysms very easy (cf. Plate XII).

CHAPTER 19

DIFFERENTIAL DIAGNOSIS FROM OTHER (PATHOLOGICAL) CONDITIONS

To discuss adequately the differential diagnosis of intracranial tumor would necessitate a survey of almost the whole field of nervous diseases, because few indeed are the intracranial diseases which do not at one time or another simulate tumor. *The differentiation of brain-tumor is made with the sum total of one's knowledge of neurology.* We can note only the most important conditions to be distinguished.

Formerly the clinician was greatly preoccupied with the differentiation of cerebral syphilis, but as this disease becomes better understood and new methods of treatment and diagnosis are developed it is less often confused with brain-tumor although it must still always be excluded in the differential diagnosis. Tuberculosis also has diminished in importance since proper care of tuberculous patients has become so universal. *At the present time, when we do not so often wait for the symptoms of intracranial hypertension and an attempt is made to establish the diagnosis of tumor early, I have found it most difficult to differentiate PRIMARY VASCULAR DISEASE of the brain.* It is not only that tumor may simulate arteriosclerosis, with multiple small vascular insults, but major apoplexy may also occur in cases of tumor. I have here the brain of such a case. You see that there is a diffuse tumor in the left angular gyrus and subjacent tissue into which a hemorrhage has occurred (Fig. 146).

The patient (CASE LVII) was an engineer of fifty-five years, apparently in perfect health. No evidence of symptoms of illness previous to February 13, 1931, could be obtained. While eating his lunch that day in the cab of his engine he suddenly fell unconscious. He recovered consciousness after about four hours but remained irritable, confused, and depressed. Wassermann reaction on the blood was negative; the bloodpressure was 230/120. Some days later, after rest in bed, it went down to 180/115. He attempted to return to work but could not interpret signals. He had great difficulty in reading. He was also unable to play cards; his memory for recent events was poor; he felt that he was about to lose his mind and wept frequently.

On March 20 the pupils were found to be normal. There was no edema of the optic discs, and no sclerosis of the retinal arteries. By gross examination there seemed to be a right homonymous defect in the visual fields. There was a right hemiparesis and hemihypesthesia. The bloodpressure was 170/94. There was no evidence of uremia. The pressure of the spinal fluid was 269 mm. of fluid in the recumbent posture. The spinal fluid was normal. After the spinal puncture the hemiparesis

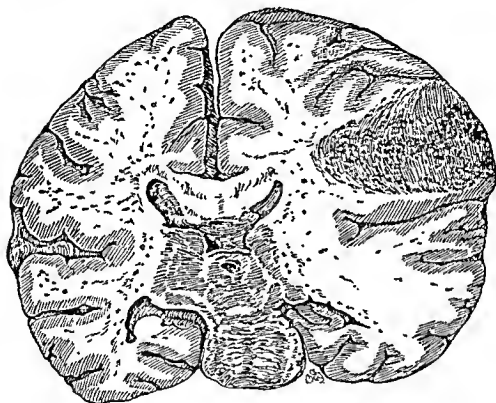


Fig. 146. Cross section of brain of CASE LXVI. Section passes through anterior part of lesion in neighborhood of left supramarginal gyrus.

increased, the patient developed a hyperpyrexia and pulmonary edema and died. The necropsy disclosed the tumor you have just seen.

There was no reason in this case to diagnose cerebral tumor before the spinal puncture was made, except that, as I have so often told you, tumor must always be suspected as a possible cause of any vascular insult in middle life. In this case the hemorrhage occurred before the tumor had reached a size to cause symptoms of increased intracranial pressure. The opposite situation may also exist; headache and choked

disc may develop before the hemorrhage or thrombosis occurs and at necropsy no tumor be found. Whenever in these cases the bloodpressure is high it is best to treat the patients as primary vascular lesions because craniotomy in cases of hypertension usually ends in a fatality from cerebral hemorrhage. I have already on several occasions discussed the difficulties of differentiating primary vascular disease from brain-tumor so I will spend no more time on this subject now, but content myself with again emphasizing its importance.

The diagnosis of SYPHILIS has been singularly simplified by the development of the Wassermann reaction. Although it cannot be always depended upon to diagnose lues, its use enables us routinely to identify syphilis in most cases. When formerly intracranial operations were so dangerous every patient with symptoms of intracranial tumor was subjected to a long course of antiluetic treatment. This procedure was justifiable at that time because the only hope of improvement lay in the possibility of the lesion being luetic. But as intracranial surgery was developed vigorous protests arose (279) against this method of procedure, so that now antiluetic treatment is given only when a reasonable possibility of lues of the brain exists. Some idea of the equivocal situations which may arise may be gained from the study of these two patients.

The first patient (CASE LVIII) is a salesman of forty years who had suffered for many years from diabetes mellitus which was treated intermittently with dietary measures. About five months ago he became nauseated and vomited. Two days later he had a severe headache in the frontal region. Since that time the headache has been practically constant with frequent vomiting. He was found to have sugar in his urine and was treated with insulin. His headache improved but his eyesight began to fail.

When admitted to the hospital four months ago he was quite jocular and apparently not worried in the least by his troubles. He admitted having had gonorrhea at the age of eighteen and again at twenty-four but denied lues. He was married, but his wife had never been pregnant. His attitude contrasted strongly with his actual condition. Vision was reduced to 0.6 in the left eye. Both discs were choked at least five diopters with large hemorrhages extending far out into the retinae. The blind-spots were very large and the visual fields greatly constricted. There was a paresis of the left third nerve, possibly also of the right seventh. No pyramidal symptoms were found and general sensibility

seemed intact. Wassermann reaction on the blood was very strongly positive. There was a trace of sugar in the urine and the blood-sugar was 196 mgm. per 100 ccm. A roentgenogram of the head showed the pineal body to be displaced nearly a centimeter to the right of the midline.

The diabetes could not account for his symptoms. It seemed most probable that there was a tumor in the left frontal lobe. On account of the Wassermann reaction it was possibly a gumma. Because of the serious condition of his eyes exploration with decompression was advised but refused, so treatment was begun with bismuth and iodides, with dietary control of his diabetes, and he was discharged. His improvement was at first slow but now, three months later, he is able to return to work as a salesman. His visual acuity is 0.6—3 in the left eye and 1.2 with the right. The paresis of the left third nerve has disappeared. The fundi have completely subsided leaving some scars and secondary atrophy. There is no glycosuria. The Wassermann reaction of the blood is still strongly positive. Roentgenogram shows the pineal body to be exactly in the midline.

With his eyes in such a precarious state this patient took a great risk in refusing operation. Secondary optic atrophy might have begun at any time and his vision have been irreparably lost. Surgeons first began to protest because neurologists persisted in continuing antiluetic treatment until the patients were blind before they were sent for operation. As a matter of fact the antiluetic treatment is often not so effective, as the following patient will demonstrate.

She is a young married woman (CASE LIX) of twenty years who began six months ago to complain of headache, frontal in location, and worse in the morning. Frequent vomiting accompanied the headaches. A Wassermann test on the blood and spinal fluid at that time was found to be strongly positive. At this time also there was moderate swelling of the optic discs. Antiluetic treatment was begun and continued vigorously but without improvement. She began to have attacks in which she became lethargic and was unable to speak for several hours. The pulse was very rapid during these attacks. Three months later she developed difficulty in using her right arm and leg. She also could not speak well and was brought to the hospital.

When admitted she was cooperative and seemed to understand well what was said to her but had great difficulty in speaking. The pupillary reactions were normal. The optic discs were choked 3-4 diopters; the

visual fields normal. There was a right hemiparesis, predominating in the arm, with extensor plantar reflex and clonus at the ankle. The right abdominal reflex was not obtained but sensation seemed normal on the right side. A Wasserman test on the blood was again strongly positive. Roentgenogram of the head was normal.

A diagnosis of gumma of the brain was made and a left osteoplastic exploration performed. The dura mater was tense. The arachnoid membrane was tough, thickened, and milky. The convolutions were not flattened. There was a great deal of subarachnoid fluid. An exploring needle found no evidence of tumor but the cerebrum seemed tougher than normal. Some fluid was removed from the lateral ventricle. A subtemporal decompression was made and the wound closed. The next day her speech was no worse but she was entirely unable to move the right arm. Motion did not begin to return until a month later. The decompressed area bulged slightly. Antiluetic treatment with mercury and iodide was continued vigorously. It is now five months after the operation. Her speech is entirely normal. The hemiparesis is markedly improved; there is still some slight weakness of the arm. The optic discs are flat and so is the decompression. The Wassermann reaction is still strongly positive.

It has been demonstrated many times that lues of the brain which has not responded to medical treatment may do so promptly after a craniotomy has been made (337). The explanation is not certainly known but the fact is sufficiently attested. Moreover, operation in these cases is attended with a very small mortality provided it is made with local anesthesia. Patients with cerebral lues take general anesthesia badly (312). So that in case prompt improvement does not occur, or in case the symptoms progress under treatment, operation should be undertaken at once. The foregoing statement applies only to cerebral lues of the meningo-vascular or gummatous variety.

Lues may affect the intracranial structures in various ways (250). It may rarely produce a simple meningitis with headache and stiffness of the neck and papilledema. In these cases involvement of the nerves is indicated by double vision, girdle-pains and dysesthesias. Lumbar puncture reveals many lymphocytes in the spinal fluid and the Wassermann reaction is strongly positive. But usually the meningitis is of the gummatous variety and involves the cortex of the brain also to form a meningo-encephalitis. Such lesions are usually said to be most common over the base of the brain but are also frequent over the convexity.

especially along the lateral and central fissures. Basilar luetic meningitis has many symptoms in common with intracranial tumor. Headache, giddiness, and vomiting are rarely absent. These patients get into a semi-somnolent, semi-comatose state difficult to distinguish from the stupor of intracranial hypertension. They seem, however, to be usually better oriented and better aware of their situation. There occur also marked oscillations and remissions in their mental states, and occasionally acute exacerbations of delirium. Visual trouble of some kind is almost universal, varying from choked discs (509) through optic neuritis and postneuritic atrophy to simple primary optic atrophy. Defects in the visual fields are very frequent. But most common is unilateral involvement of the oculomotor nerve producing especially ptosis of the upper eyelid. Any of the other cranial nerves may be affected, but less frequently, the favorite site for the gummatous lesions being the region of the optic chiasm and interpeduncular space. It is evident that the clinical picture produced may simulate closely that of basilar neoplasms. Yet even in the atypical cases a careful history may make one suspect lues. In addition to headache the prodromal symptoms of intracranial lues include often marked disturbances of sleep, shivering attacks with low fever, pachy anesthetic areas due to involvement of dorsal roots of the nerves, abnormal pupillary reactions and disturbances in micturition. When the meningoencephalitic process involves the cortex over the vertex, epilepsy, aphasia and other focal symptoms may be produced, which progress gradually in exactly the same way as those produced by cortical neoplasms.

But lues does not confine its attack to the meninges. The arteries also may be primarily affected. The process may attack the larger arteries causing massive fibrous proliferation of the intima with splitting and reduplication of the elastica, more or less proliferation of the endothelium, and usually a lymphocytic or gummarous periarteritis. The periarteritis may be absent in chronic luetic vascular disease. Less commonly changes occur in the vessels which can with difficulty be distinguished from those of ordinary arteriosclerosis; there is thickening and hyperplasia of the connective and elastic tissues especially in the intima, accompanied by fatty infiltration of the intima, hyaline change in the arterioles and primary calcification of the media of the larger arteries. Rarely the pathological process affects the cortical capillaries producing an endarteritis with proliferation of the endothelial and adventitial cells. But whatever the nature of the arteritis, the symptoms progress

in episodes just as in arteriosclerosis, and for the same reasons, and the differentiation must be made from this disease and from cerebral neoplasm, especially glioblastoma multiforme. Syphilitic cerebral vascular disease is usually accompanied by headache, giddiness, and vomiting, often also optic neuritis or even choked discs. The age-incidence is a little different from arteriosclerosis, being usually from twenty to thirty-five years, whereas arteriosclerosis predominates from forty to sixty, but there is rough overlapping as may be supposed.

Cerebral vascular lues is usually readily identified by the Wassermann reaction, which is almost invariably positive in the blood and often in the spinal fluid also. The variability of the reaction in the spinal fluid seems to depend on the extent of the involvement of the meninges. Basilar luetic meningitis is also usually identifiable by means of the Wassermann reaction in blood and spinal fluid. But gummatous intracranial lesions may exist with a completely negative Wassermann reaction in both blood and spinal fluid. When you realize that on the contrary a positive Wassermann reaction on the spinal fluid in cases of actual intracranial neoplasms is not rare (344), the difficulty of differentiation is apparent. You must remember also that there is nothing to prevent a luetic patient from developing a cerebral neoplasm.

Gummatous tumors generally start in the meninges although they may originate in the skull itself. From the meninges the inflammation spreads along the perivascular tissues into the cortex of the brain (103). It extends outwardly also when situated over the vertex, involving the dura mater and often also the calvaria. Over the base of the brain the dura mater is usually unaffected. When the skull is opened the dura mater is found to be elevated, roughened, and discolored over the gumma; it is, moreover, adherent to the underlying cortex. The gumma separates with difficulty from the brain, leaving a roughened, warty surface. Its consistency varies greatly in different parts from a gelatinous softness to a firm rubbery texture. When cut in cross section the peripheral parts are pinkish and softer, contrasting with the firm yellowish-gray central regions (Fig. 147). In the larger lesions the center may be necrotic. Gummatous meningitis and arteritis usually accompany them. Gummas vary greatly in size and are seldom single. They are very resistant to antiluetic medical treatment.

Lues may affect also the parenchymatous tissue of the brain primarily, causing dementia paralytica. The clinical manifestations in these cases may begin with epileptic attacks or rarely with cerebellar

disturbances before marked dementia ensues. We have learned also that tumors of the frontal lobes may cause mental symptoms closely resembling those of general paresis. But the latter disease may be almost invariably identified by examination of the spinal fluid. A diagnosis of general paresis when the spinal fluid is normal should always be

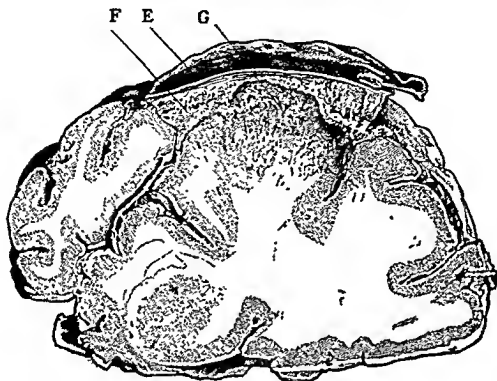


FIG. 147. Cross section of brain with gumma, G—involve ment of brain, E—thickened and adherent dura mater, F—gummatous proliferation of the leptomeninges (after Bramwell).

suspected and another cause than lues be sought to explain the symptoms.

The other frequent infectious granuloma is the TUBERCULOMA. Toward this lesion also our attitude has radically changed in the last half century. Tuberculoma was formerly considered to be in children equally as frequent as neoplasms, and in adults (over nineteen years of age) it was said to be quite common (13.6 percent of all brain-tumors) (455). Although still four times as frequent in children as in adults, today tuberculoma is a rather uncommon intracranial lesion in the United States although much more frequent elsewhere, certainly

not one-tenth as numerous as neoplasms in children and rarely found in adults. It is important to recognize it, however, because the results of operation are not good.

. This patient (CASE LX) I am sure has a tubercle in the cerebellum. He is a thin, emaciated young man of twenty who has always been delicate. Ten years ago he had influenza followed by pneumonia. Two years ago he was ill for three months with pleurisy and effusion. He began about one year ago to have a pressure-like pain in the occipital region at the base of the skull. At first it came only once a month but gradually more frequently. It began in the morning and became so severe that he was frantic. Occasionally he lapsed into a stupor. The pain radiated up over the left side of the head. There was no nausea or vomiting. Six months ago he had to give up his work because he could not pick up small objects with his left hand. This difficulty grew steadily worse. He noted also a tendency to stagger to the right when walking. For about the same time there was at times a roaring noise in the right ear. Two months later his vision began to be blurred and in the last three months he had lost ten to twelve pounds in weight and became very weak.

When admitted to this clinic he was found to be feeble and emaciated. There was a rather extensive proliferative tuberculosis in the apices of the lungs. He had no cough and his temperature ranged between 36.5° and 37.2° . He held his head tilted to the right. Just back of the right mastoid process could be heard at times a swishing noise synchronous with the heart-beat. In walking he deviated more often to the right. There was a nystagmus on looking to the right and left, coarser and slower on looking to the left, with a clockwise rotatory component. The optic discs were elevated four diopters with marked secondary atrophy. Vision was 0.1 with the right eye and 0.4 with the left. The visual fields were generally constricted. There seemed to be slight left facial weakness. Auditory acuity was slightly diminished in both ears; the vestibular apparatus functioned normally on both sides. There was a slight bilateral exophthalmos (right 21, left 20.5). The extremities were all hypotonic and the tendon-reflexes were obtained only by strong reinforcement. There was an action-tremor of the left arm; some asynergia and hypermetria of the left arm and leg; rapid alternate movements were badly made with the left hand. Roentgenogram of the head showed some absorption of the sella turcica. The symptoms pointed to a tumor of the left cerebellar hemisphere although the his-

tory and finding of staggering to right, together with the occasional bruit back of the right ear, indicated the possibility of a lesion also in the right hemisphere. Because of the pulmonary tuberculosis a tuberculoma was most probable although a hemangiothlastoma was also considered because of the bruit.

A suboccipital craniectomy was made with local anesthesia. As soon as the dura mater was opened it was evident that there was a large mass

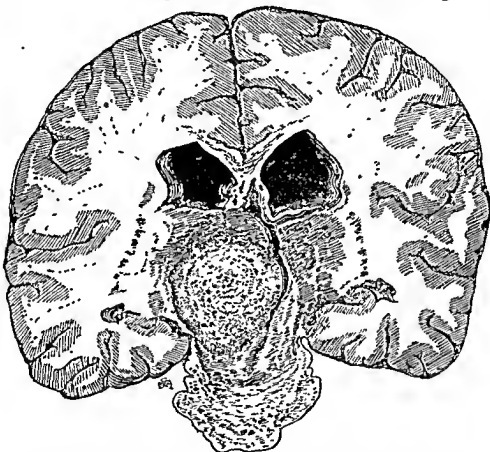


FIG. 148. Cross section of brain with tubercle in the left cerebral peduncle.

in the left hemisphere. The vermis was pushed far over to the right. The left tonsil was herniated into the foramen magnum. The left hemisphere was very hard and adherent to the dura mater laterally. Since the lesion was almost certainly a tubercle the wound was closed without any attempt to remove it. He recovered promptly from the operation. His headaches are relieved; his choked discs have subsided, but his cerebellar symptoms are unchanged, as you see. The nystagmus

is marked, he cannot walk without assistance and is to be transferred immediately to a sanatorium for tuberculosis.

Tuberculosis causes most frequently two very different affections of the nervous system—tubercle of the brain and tuberculous meningitis. Rarely a chronic tuberculous thickening of the meninges in a circumscribed area may occur (meningitis chronica tuberculosa circumscripta) or small tubercles be found in the meninges in cases of acute miliary tuberculosis, but usually tuberculous meningitis is a diffuse affair for which nothing can be done. Tubercles of the brain are often multiple, but solitary ones occur (Fig. 148) and are said to be most frequent in the cerebellum. There is some doubt about this localization. It is perhaps more accurate to say that those which are suspected of being tumors are most often in the cerebellum, since solitary tubercle in the cerebrum rarely causes signs of intracranial hypertension.

Patients with tubercles in the brain usually die of tuberculosis elsewhere in the body, often miliary tuberculosis (237). Sometimes the cerebral tubercle will approach the meninges causing a terminal tuberculous meningitis. Tubercle of the brain may be suspected when symptoms of a focal lesion of the brain without symptoms of increased intracranial tension develop in a child with tuberculous lesions elsewhere in the body. There is no way of making a positive diagnosis before operation. At the present time cerebral tubercle is much more frequent in negro than in white children. At operation tubercle may be suspected from the hardness of the lesion and is more certain if the lesion also involves the meninges, as in the case I have just shown you. It is then much better to leave it alone. Any attempt at extirpation is often followed by a tuberculous meningitis (484). A decompression will give immediate relief and the patient should then be treated like a case of general tuberculosis.

In this country PARASITES do not often enter into a differential diagnosis of intracranial disease but occasionally they are encountered. In many foreign countries hydatid disease must always be considered. It would be wise for us also to remember this possibility whenever we have patients of foreign birth. All of the cases of intracranial echinococcus infection which I have seen have been born abroad, usually in Greece. Hydatid disease of man is caused by the cystic stage, in the intermediate host, of the taenia echinococcus which normally infests the intestine of dogs (170). Man is infected by ingesting the ova; the embryo is hatched in the stomach or upper intestine and penetrates

its wall. It is, therefore, understandable that the cysts are more frequent in the liver than in any other organ, since it is the first organ to which the venous blood carries the embryos. In man the cysts of the brain may be either *primary* or *secondary*. In the former case the embryo passes through the liver and lungs and lodges in the brain. Such pri-

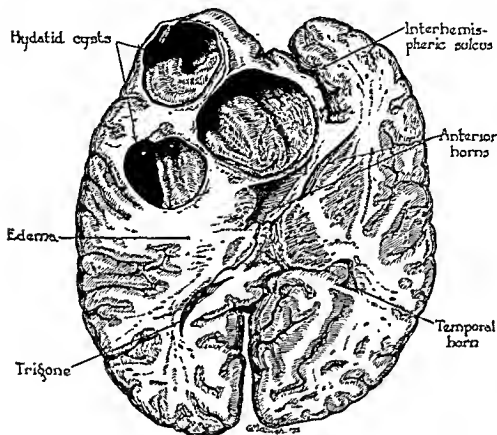


FIG. 149. Horizontal section of brain which hydatid cysts (after Kaufmann).

mary cysts of the brain are rare and much more frequent in children than in adults. They are almost always solitary and may reach an enormous size, containing as much as nineteen ounces of fluid. The cyst has a very thin wall and causes very little reaction in the surrounding cerebral tissue. It is almost always in the cerebral hemisphere. The secondary cysts are merastatic and usually multiple (Fig. 149). They may occur anywhere in the brain. They result from the transportation of scolices or brood-capsules to the brain following rupture of a primary cyst usually in the left side of the heart. The cysts are typically in the

cerebral substance but may rupture secondarily into the subarachnoidal space or ventricles.

It can be understood that the symptoms resulting from such a disease of the brain will be quite varied. Almost any sort of focal symptom may occur, of which focal epilepsy is most common. Some of the patients are considered to be idiopathic epileptics, others as basilar luetic meningitis, some have no symptoms, the cysts being found at necropsy, and still others are psychotic—dementia, depression, disorientation, hallucinations, catatonia, manic excitement, and delirium, being observed. In children the cysts cause a peculiar erosion of the skull in their neighborhoods which is rather characteristic.

The diagnosis cannot be made from the neurological symptoms but is established by demonstrating a general hydatid disease (308). The cysts may be demonstrated in the liver or lungs. If not, the presence of such an infection may be established by complement-fixation test on the blood (positive in about 80 percent of cases) or by intradermal test (positive in about 90 percent to 95 percent). No constant changes are produced in the cerebrospinal fluid although a paretic gold-curve may be found. Precipitin and complement-fixation tests on this fluid are very inconstant and the Wassermann reaction is negative. The nationality and birthplace of the patient are of considerable importance. The disease is contracted usually in childhood and is especially prevalent in sheepherding communities where the hygienic conditions are not so good. It is most common in certain parts of Australia, South America, South Africa, and southeastern Europe.

In addition to arteriosclerosis, syphilis, tuberculosis, and hydatid cysts there is a host of conditions less frequently confused with intracranial tumor. I can mention only a few of them. BRAIN ABSCESS, if it develops in immediate sequence to an acute infection of the middle ear, accessory nasal sinuses, or in the course of a chronic bronchiectasis or abscess of the lung is usually readily diagnosed. But sometimes the intracranial extension of the infection may pass unobserved in the course of the primary affection and it is with these chronic abscesses that difficulty in diagnosis arises (17).

Except for frequent sore throats this boy (CASE LXI) of fifteen was well until eight months ago. He had at that time a cold and was in bed with a discharging right ear for a week. Then he had spells of crying and convulsive seizures and complained of pain and a pulsating sensation in the occipital region of his head. He did not arise from his

bed until a month later and soon began to complain that he did not see well. He was examined at this time and found to have choked discs of five diopters. His parents were advised that he probably was suffering from a tumor of the brain, but they refused to consider an operation. A month ago he became almost totally blind and was finally brought to this hospital.

When admitted he was irritable and uncoöperative at times. There was secondary atrophy of both optic discs which were also elevated about four diopters. He could recognize moving objects with the right eye only. Examination of the visual fields was of course impossible. He was very unstable emotionally but no localizing symptoms could be found. His temperature ranged from 36.5° to 37.4° . Leucocyte-count was 6600. No localizing symptoms being found a ventriculogram was made. The ventricular system was not much distorted but was displaced markedly to the left. The gold-curve on the ventricular fluid was 4 4 5 5 1 1 1 0 0 0. There was a trace of globulin in the fluid. The cells seem not to have been counted. The possibility of abscess was considered because of the subnormal temperature and history of infection but was thought improbable. There was a perforation of the right tympanic membrane but no discharge.

A right osteoplastic craniotomy was therefore made. The *dura mater* was very tense. The convolutions in the temporal region were flattened, yellowish, avascular, and soft. The lateral fissure was displaced upward. A longitudinal incision in the first temporal convolution came down on a firm mass which separated readily from the brain. It was attached only to one spot on the petrous bone. Some bleeding from this place was stopped with muscle. The tumor was thought to be a meningioma although at the time of operation it was remarked that there had been unusually little bleeding. Examination of the specimen showed it to be an abscess with a very thick wall. Its contents were sterile, but it had been for two days in formalin before being opened. The patient developed a septic type of fever, ranging from 37° to 39.8° . Three days after operation puncture was made in the temporal region and a drain was inserted. There was a serous discharge from which no organisms were grown. The temperature gradually subsided. The drain was removed a week ago and he is now quite well. The choking of his optic discs has subsided, but his vision is permanently lost.

Whenever in the previous history of a patient with intracranial hypertension there occurs an acute febrile episode of any nature the

patient and his relatives should be questioned closely concerning symptoms at that time which might indicate an intracranial extension of the infection. Intracranial suppuration is often initiated by a chill; this may be a frank chill or only a vague chilly shivery feeling. Headache is almost always present varying from a dull ache to a violent pain. True projectile vomiting rarely occurs but irregular vomiting is often present. Malaise and prostration out of proportion to the external suppuration are also suggestive. When these symptoms occur after the primary

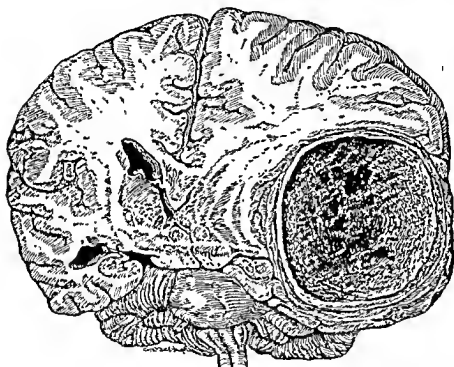


FIG. 150. Cross section of brain with encapsulated abscess in left temporal lobe.

febrile disturbance has disappeared, whether an operation has been performed or not, intracranial extension should be feared. When the intracranial suppuration is active the symptoms vary with the extent of involvement of the meninges. When the meninges are involved there is always a pleocytosis in the spinal fluid, largely polymorphonuclear leucocytes in the invasive stage.

Chronic abscess (Fig. 150) may be suspected from the history, from a subnormal irregular temperature or pleocytosis in the spinal fluid.

There are often convulsions, especially in children. The pulserate tends to be slow even when the intracranial tension is not increased. *Indeed a slow pulse is much more characteristic of abscess than of tumor, except in acute exacerbations of intracranial hypertension.* Projectile vomiting may also occur if the abscess is in the cerebellum, even when the intracranial tension is not increased. Palsy of the sixth nerve is frequent and of no localizing significance; it is often involved in the supuration where it passes over the tip of the petrous bone. Papilledema is rare if the abscess is in the frontal lobe; mild homolateral papilledema often follows occlusion of one lateral sinus or jugular vein; bilateral papilledema is most frequent with cerebellar abscess.

The results of CRANIAL INJURY are sometimes very confusing. A story of a blow on the head can almost always be obtained in any case of intracranial neoplasm if it be asked for. The history of cranial injury must be accepted with caution, especially since we have compensation-laws for workmen. Repeatedly in my experience the symptoms of cerebral tumor have been dated from some trifling injury received while at work. The student must realize that many patients, either wittingly or unwittingly, may distort the clinical history and so mislead the physician. He must learn to judge the reliability of the patient as a witness. Even when there is no question of misinformation it is not always easy to determine the exact state of affairs especially in those cases of slow formation of a subdural hematoma which may follow trifling injuries.

This man (CASE LXII) of forty-nine was brought to the hospital in a semi-comatose condition. His relatives related that a month ago he complained of headache over his right eye. Before this time he had been well but somewhat depressed since his brother's death three months previously. Headache continued for a week when he called a physician for the first time in his life. The physician gave him some powders for his headache, but it was not relieved. On the evening before his admission to the hospital he ate heartily but soon began to be drowsy and asked foolish questions. The following morning he was worse, had to be helped to the bathroom, and was later brought to this clinic.

When admitted he could not be aroused sufficiently to answer questions intelligently. His pulserate was 80 and his bloodpressure 110/64. The right pupil was larger than the left but both reacted to light. The fundi were normal. The right abdominal reflex was not obtained and the knee-jerk was brisker on the right side. There was no sugar in the

urine and no albumen. The temperature was 37.2° by rectum. On the following morning his pulse rate had fallen to 40 but the blood pressure had risen only to 118/74. The right pupil was still larger. The tendon-reflexes on the left side seemed slightly brisker. No abdominal reflexes were elicited. There was some cervical rigidity. A lumbar puncture was made; the pressure was 550 mm. of fluid, and the fluid was clear but slightly yellowish. Questioning of his relatives elicited only the fact that he had tripped on the lawn and fallen about the time of onset of his headaches. He did not strike his head and was not injured in any way. They knew of no other accident. Roentgenogram of the head showed no evidence of fracture. The yellow cerebrospinal fluid indicated old bleeding near the subarachnoid space, but its source and cause were not evident. However, his condition was serious and the possibility of an extradural hemorrhage made us advise exploration, on the right side because of the dilated pupil.

Under local anesthesia, therefore, a trephine-opening was made in the right temporal region. As soon as the dura mater was opened a large quantity of chocolate-colored fluid escaped. A fragment of the dura mater was removed. On its under surface was about one mm. of a reddish-gray material of about the consistency of liver. A drain was inserted and a bandage applied. The pulse rate rose to 80 on the following day and the blood pressure fell to 102/60 but two days later the patient could not be roused, the pulse rate gradually descended to 55, and the pressure rose to 112/78. It was considered possible that he had a similar hematoma on the opposite side, so a trephine-opening was made on the left side. No hematoma was found; the brain was not tense. After this he slowly improved, the pulse rate varying between 55 and 90. He complained a great deal of headache. There was considerable bloody discharge from the drain, but that has now ceased and he is quite well and ready to be discharged. He tells us now that about a month before his headaches began he fell downstairs and bumped his head rather badly. He was not unconscious and said nothing about it to his relatives.

✓ Chronic subdural hematoma (389) is usually unilateral but is bilateral in about a third of the cases. It is usually situated over the vertex of the cranium but may be basal and occasionally in the cerebellar fossa. The collection of blood varies in thickness from a few millimeters to four or five centimeters (Fig. 151). Complete organization of a large hematoma is rare so that usually there is a large amount of coffee-

colored fluid containing clots. The outer portion is usually organized by connective tissue and of about the consistency of liver. It is reddish-brown in color with streaks of green and red. The inner surface contains large thin-walled vascular sinuses from which fresh hemorrhages may occur. The clot is, therefore, completely surrounded by connective-tissue cells which attempt to organize it, especially from the dural surface. The outer surface is sometimes adherent to the dura mater, which



FIG. 151. Subdural hematoma as seen at operation (from Homans).

may be discolored with greenish pigment. The arachnoid membrane is not adherent to the inner surface which is usually yellowish in color.

Alcoholism is thought to be a predisposing factor. A spontaneous form exists in infants (373) and is the principal lesion to be differentiated from tumor during the first year of life. But trauma to the head

is almost always the exciting cause especially in adults. It may be very slight. The bleeding may come from ruptured sinuses, lacunae, or probably most frequently from ruptured cerebral veins which traverse the membranes on their way to the sinuses. Symptoms may come on in a few hours or be delayed for weeks or months. In general the longer the latent period the more gradual is the onset of symptoms.

The symptoms are extraordinarily variable. Oculomotor palsies are frequent. From local pressure of the hematoma arise hemiparesis, aphasia and convulsions. Stiffness of the neck is common and, with increase in size of the hematoma, headache, vomiting, and choked discs appear. Mental aberrations are frequent and out of proportion to the intracranial hypertension. These patients are irritable, stubborn, and unmanageable, sometimes untidy and obscene. There is usually a low fever but subnormal temperatures are common and these combined with a slow pulse, also frequent, often make one suspect cerebral abscess. The spinal fluid is usually under increased pressure and often of yellowish color.

✓ One of the lesions usually mentioned in any discussion of differential diagnosis is ANEURYSM. Yet intracranial aneurysm of sufficient size to cause intracranial hypertension is rare. It is usually stated that one of the characteristic symptoms of intracranial aneurysm is a bruit to be heard over the head. This is not true in my experience. An intracranial bruit is heard whenever there is an arteriovenous fistula within the cranium. This occurs often in the presence of angioma, rarely with aneurysm. By aneurysm we mean a focal, fusiform, or saccular dilatation of an arterial wall or a saccular cavity communicating with the lumen of an artery. It may be embolic or traumatic, occasionally of syphilitic origin, but in young people it is usually due to a congenital defect in the arterial wall (201). In older people aneurysms are often of arteriosclerotic origin. Congenital aneurysms predominate between the ages of twenty-five and fifty years and arteriosclerotic aneurysms after fifty years of age. Both types are most frequent at the branching of the cerebral arteries near the circulus arteriosus. Syphilis causes aneurysms of the larger arteries; in the smaller ones the proliferation of the intima which it causes occludes the lumen before the wall is sufficiently weakened to result in an aneurysmal sac. Hence in the brain syphilitic aneurysms are common in the basilar artery. Intracranial aneurysms are not very frequent; perhaps in 0.80 percent of examinations of the head they are found, infectious in 0.24 percent and noninfectious in 0.57 percent.

The symptoms of intracranial aneurysms are rarely due to their size. *Direct rupture of an aneurysm causes apoplexy and death. But most characteristic is a seeping of blood from the aneurysm or repeated partial ruptures (Fig. 152) which give rise to a typical intermittent course of events (5).* The symptoms in the successive attacks vary with the extent of the hemorrhage. There may be a severe headache with some stiffness of the neck and fever which lasts for a few days only. There

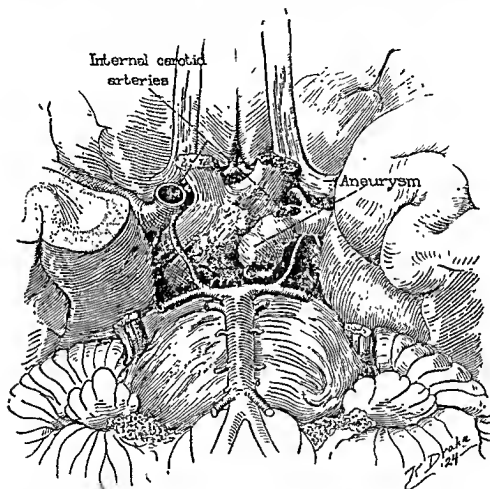


FIG. 152. Ruptured aneurysm of the right middle cerebral artery (from Parker).

may also be dizziness, apathy, drowsiness, delirium, or, if the hemorrhage be extensive and sudden enough, an apoplectic attack with or without hemiplegia, coma, and death. When such attacks occur successively at irregular intervals aneurysm should be suspected. The diagnosis is aided by finding blood in the spinal fluid early in the attack and

can be definitely established by arteriography (346, cf. Plate xv). In older patients hemorrhage into the subarachnoid space or ventricles in the absence of aneurysm, or hemorrhage into a tumor, usually glioblastoma multiforme, cannot always be excluded. However, palsies of the cranial nerves increase the probability of aneurysm since it lies so frequently around the circulus arteriosus. In particular the common congenital aneurysm of the internal carotid artery and its immediate branches gives rise to a syndrome characterized by palsy of the oculomotor nerve and severe supra-orbital pain due to involvement of the ophthalmic branch of the trigeminal nerve.

Various types of ENCEPHALITIS simulate intracranial tumor. Many tumors run an irregular temperature and without signs of intracranial hypertension are diagnosed as encephalitis (459). On the other hand encephalitis may produce signs of increased intracranial tension and lead to surgical intervention for tumor. The term encephalitis implies inflammation of the brain, and has been badly misused. The brain has a rather stereotyped way of reacting to injuries, which is perhaps the reason why of all the non-suppurative encephalopathies called encephalitis only two have a known infectious agent. If we exclude syphilis, tuberculosis, parasites, and sepsis, which we have already discussed, we may classify non-suppurative encephalitis as follows (236):

1. Chronic multiple sclerosis and certain acute cases of multiple sclerosis.
2. Acute disseminated encephalomyelitis and certain cases of acute multiple sclerosis.
3. Cowpox and rabies vaccine, measles, varicella, variola, and certain varieties of disseminated encephalomyelitis.
4. Encephalitis periaxialis diffusa and disseminated encephalitis.
5. Rabies, epidemic encephalitis, and polioencephalitis.
6. Toxic encephalitis secondary to acute infections and exogenous toxins such as lead.

In all these conditions the details of the pathological changes differ, but many are with difficulty distinguished from each other and of many the cause is unknown. Each of them may simulate intracranial tumor.

We have already noted how with some tumors, particularly in the basilar regions of the brain, may occur fever, pleocytosis in the spinal fluid, somnolence, delirium, and palsies of the cranial nerves. Conversely, with many degenerative and infectious diseases of the brain, fever and pleocytosis may be absent and symptoms of intracranial ten-

sion appear. The diagnosis is established in such cases from accessory data or from the appearance of more or less specific signs of a particular malady. Even the most experienced neurologist may remain in doubt of the correct diagnosis.

Formerly among workers in various industries using lead, cerebral symptoms frequently developed (75). Severe headaches and convulsions, intense double optic neuritis or occasionally amaurosis without edema, strabismus, dilatation and sluggishness of the pupils to light, mental aberrations, even violent excitement and coma in fatal cases, were some of the symptoms observed. Aside from the history of working with lead the diagnosis was established by the presence of a blue line on the gums, anemia, abdominal colic, constipation, wristdrop, and by the presence of lead in the feces. Such conditions at the present time are fortunately rare because workers are better protected, but lead-poisoning is occasionally seen, in my experience always in children (356), and usually from chewing the paint off their cribs.

It would be impossible for me to discuss with you each of the more or less well-known types of encephalitis. Such a discussion would take us too far afield. Moreover, in my experience, tumors which have simulated some form of encephalitis have been almost invariably inoperable. But I should like to call your attention to the fact that there exists in addition to the more or less well-known varieties of degenerative and inflammatory diseases of the brain a great number of encephalopathies of unknown nature which may simulate intracranial tumor. These are apt to be called pseudotumors (206) by the surgeon who has his attention fixed on the possibility of tumor, or CHRONIC SEROUS MENINGITIS and chronic arachnoiditis (272) because at operation he finds some thickening of the leptomeninges with local accumulations of cerebrospinal fluid. Many of these cases are doubtless due to obscure inflammations of the brain of unknown nature (29). Something similar is often produced in children following infections of the middle ear and mastoid cells.

This woman (CASE LXIII) of thirty-two years is typical of these obscure conditions in their acute stages. She came to the clinic complaining of failing vision. Four months previously she had begun to have headaches, mainly in the frontal region. She consulted a physician at this time who found her vision in the left eye to be very bad; the right vision was good. Her condition changed little until three weeks ago when she began to have what she calls "misty spells" during which

for a few seconds she could not see clearly. She became forgetful and depressed. She had previously been well but was always fat, even as a child, weighing over two hundred pounds since reaching adult life. For the last four years her menses were irregular. She had been married for six years and had never been pregnant. But she had never been ill except with children's diseases and an appendicitis for which an operation was performed five years previously.

When admitted to the clinic she weighed 111.4 kg. and was 167.5 cm. in height. Her bloodpressure was 132/90. The basal metabolic rate was +1. The urine and blood were normal. General physical examination was normal. There was no indication of any organic lesion of the nervous system apart from the eyes. Roentgenogram of the head showed the optic canals, accessory nasal sinuses and sella turcica to be normal. Both optic discs were markedly choked, the right being elevated two diopters and the left between three and four diopters. There were numerous hemorrhages over each optic disc. The visual acuity of the right eye was 1.5—1 and of the left eye 1.0+2. The visual fields were normal. Although the acuity was so good the periods of amblyopia indicated that the vision might be suddenly lost. In the absence of any localizing signs it was decided to make a ventriculogram, since it seemed reasonably certain that a brain-tumor was the cause of the visual disturbance.

The ventriculogram to my surprise revealed a perfectly normal ventricular system (the fourth ventricle was not seen). It is now five months since the ventriculogram was made. Nothing has been done for her except to extract some abscessed teeth, but she has ceased to have blind spells. Her vision in the left eye is 0.8+1 and in the right eye 1.5—4. The swelling of the optic discs has subsided; there is only slight edema of the left disc, the right is normal. Although the blind-spots are considerably enlarged the visual fields are normal. She no longer suffers from headaches and considers herself to be well.

Here is also a child (CASE LXIV) who must have some similar trouble. He is four years of age and was taken ill two months before his admission to the hospital with an attack of vomiting. The vomiting recurred a week later and at that time he complained of headache. The attacks of headache and vomiting increased in frequency and severity. He would scream with pain and hold his head between his hands. His extremities were very hypotonic and the tendon-reflexes were very feeble. There was never any swelling of the optic discs. The

middle ears were always normal. Only a slight acidosis was found, doubtless due to repeated vomiting. Cyclic vomiting with acidosis was considered as the most probable diagnosis although the severity of the headache kept the physician on the lookout for symptoms of tumor. However, the sutures were not separated, the neck was not stiff, there was no disturbance of gait and the optic discs were not swollen until two months had elapsed.

When admitted he was very irritable and restless. There was no "cracked-pot" sound when the head was percussed and a roentgenogram showed no separation of the sutures. There was slight swelling of the optic discs and no nystagmus. He would not cooperate well for cerebellar tests but his gait seemed normal. When playing with his toys there seemed to be some hypermetria of the hands. All of his extremities were very hypotonic and the tendon-reflexes were very weak. Shortly after admission he had an alarming attack of headache and vomiting with stiffness of the neck and the swelling of his optic discs rapidly increased. It was determined to operate for possible cerebellar tumor.

A suboccipital craniectomy was made but no tumor was found. The cerebellum seemed perfectly normal. There was no herniation of the tonsils, the vermis was not full, and the hemispheres were of normal consistency. The posterior cistern was greatly dilated and the arachnoidal membrane seemed thick and cloudy. The fourth ventricle was empty. The intracranial tension was completely relieved so that there seemed no evidence of any block of the aqueduct. The wound was carefully closed. After a transitory hyperthermia the child was well for four days and then began to complain of headache and his temperature rapidly rose to 40° . The suboccipital region was very tense. His wound was opened and drained. The temperature immediately subsided and he was quite well for a couple of days when one evening the nurse reported that he had a fever again. The drain was found to be occluded. Opening of the drain was followed by prompt subsidence of the temperature. Thinking that possibly there might be a tumor in the third ventricle an encephalogram was made which showed a perfectly normal ventricular system and subarachnoid space. Six days following the encephalogram the wound was allowed to close, the temperature did not rise, and he has since remained well.

I believe that these obscure intracranial conditions result, in their chronic form, in the condition called by neurologists chronic serous

meningitis and by neurosurgeons chronic arachnoiditis or pseudotumor. The cerebral affection is accompanied by a meningeal inflammation which results in some thickening and interferes with the proper circulation of the cerebrospinal fluid. Of course the finding of arachnoidal thickening and adhesions by the surgeon does not prove that there is no tumor; often the tumor is found at necropsy in another situation. But a sufficient number of necropsy-reports exist to prove that such arachnoidal adhesions may be present when there is no tumor and I believe they are secondary to encephalic affections, the nature of which is at present obscure. The primary disease may have been forgotten or have provoked such slight symptoms as to pass unperceived, while the secondary arachnoidal thickenings by compression of nervous structures or by impeding circulation of cerebrospinal fluid first attract the attention of the physician.

It is impossible in the short time at my disposal for me to teach you how to differentiate all of the multifarious conditions which may simulate intracranial tumor, but perhaps I have sufficiently impressed you with the difficulties of diagnosis in many intracranial pathological conditions. The more one knows of medicine in general and of neurology in particular the fewer mistakes he will make. Yet the best trained clinician will often err because our ignorance of many of the diseases with which we must deal is abysmal. *It is best when in doubt to treat an uncertain condition as tumor*, because for tumor something may be done whereas for most of the diseases simulating tumor there is no effective treatment. Even for lues, as I have indicated, operative treatment is sometimes necessary and effective.

TREATMENT OF INTRACRANIAL TUMORS AND ITS RESULTS

There is only one rational treatment of intracranial neoplasm and this is to remove it by operation as soon as the diagnosis can be established. Alas, it is easier said than done! Although easier now than half a century ago, there are many intracranial tumors which it is still impossible to remove; for them accessory methods of treatment will need to be discussed directed toward reducing the increased intracranial tension, retarding the growth of the tumor or relieving distressing symptoms. In addition there will always be a certain number of tumors which we will never be able to remove, such as gliomas of the brainstem.

The number of fatalities from operations for intracranial tumor would be materially reduced were we able to foretell in every case the exact nature and location of the lesion. But up to the present time in only three specific tumors have I been sufficiently certain of my diagnosis to advise that an operation would be futile; these were glioma of the corpus callosum, glioma of the optic chiasm, and glioma of the brainstem. Ordinarily, therefore, there is only one indication for operation for intracranial tumor and this is the reasonable certainty that such a tumor exists. And there is only one time for operation and that is as soon as the diagnosis can be established. It is obvious that the earlier the diagnosis of tumor is made the easier will be its removal. Difficulties multiply as the size of the tumor increases and as it infiltrates the surrounding structures.

But we have learned that it is not only necessary to know that a tumor exists in the intracranial cavity, we must know also its location. The abdominal surgeon strives also to make a localizing diagnosis but, if he cannot, he can open the belly by a midline incision and through it explore the entire abdominal cavity. The cranial surgeon cannot do this. It is necessary for him to make his opening in the cranium accurately in a certain region for each type of tumor in a given situation. Since it is not possible to locate accurately all intracranial tumors from the symptoms alone, it is necessary at times to resort to minor operations in order to secure added information necessary to the planning of an attempt to remove the tumor.

Suppose that the physician is uncertain whether the tumor is situated in the supratentorial or subtentorial cavities. He may resort to what is known as the method of ventricular estimation (151). The two lateral ventricles are punctured and drained of their contained fluid. If considerably more fluid than normal is obtained, but an approximately equal amount from each ventricle, one may conclude that there is an internal hydrocephalus. This is most commonly caused by a tumor in the posterior fossa. But not necessarily so; a tumor in the third ventricle or near the midbrain may cause also equal dilatation of the lateral ventricles. To surmount this difficulty a dye, usually phenolsulphonphthalein, is injected into one lateral ventricle. If it cannot be withdrawn in the fluid from the opposite ventricle one, at least, of the interventricular foramina is occluded. But it cannot conversely be concluded, if the dye does pass freely from one lateral ventricle to the other, that the interventricular foramina are open, because often in cases of internal hydrocephalus large openings are produced in the septum lucidum through which fluid may freely pass, even though the third ventricle be entirely filled by a tumor. Moreover it should be remembered that with the head in the usual semiteclining position for making these ventricular punctures more fluid will be obtained from the first ventricle punctured, because not only will that entire ventricle be drained, but also the anterior part of the opposite ventricle above the interventricular foramen. One cannot necessarily conclude, therefore, because more fluid is obtained from one lateral ventricle that the opposite one is partially occluded. Nor, if the total amount from each ventricle is not increased, can one certainly conclude that the tumor must lie in a situation which does not interfere with the drainage of cerebrospinal fluid. Patients may die of intraventricular tumor and the ventricular system not be dilated appreciably. The method of ventricular estimation is, therefore, subject to many errors of interpretation.

A much more certain way to visualize the ventricles is to fill them with air and then photograph them with roentgen-rays. This may be accomplished through a needle inserted into the lumbar sac of the subarachnoid cavity. The best method uses two needles (method of Bleckwenn). The upper one is inserted between the third and fourth lumbar vertebrae and the lower one between the fourth and fifth. The upper needle is connected by a rubber-tube to the upper end of a long glass-tube of 150 ccm. capacity or more, and the lower needle

in the same way to its lower end. By lowering the glass-tube the cerebrospinal fluid will flow from the lower needle and air is automatically and simultaneously injected into the spinal canal through the upper needle. With the patient sitting, the air bubbles upward replacing the fluid first in the posterior cistern, then in the interpeduncular space, then fills the ventricular system, and finally infiltrates into the sulci over the cerebral hemispheres. This method of filling the ventricles has many inconveniences. In the first place, sometimes the air will not enter the ventricular system at all. Also, the forest of ramifying shadows of the sulci and cisterns obscures the ventricles in the roentgenogram. Moreover, the method is dangerous when there is an increased intracranial tension, especially if a tumor be present in the posterior fossa, for the same reasons that any lumbar puncture is dangerous. It has the advantage of filling the third and fourth ventricles well, but the method should never be used except in an operating-room where the necessary facilities are ready to deal with emergencies.

It is safer in cases of intracranial tumor to puncture the lateral ventricle directly and introduce the air in this way (148). To accomplish this the patient is usually placed in a semiteclining posture. Two trephine-openings are made, one in each occipital region about 3 cm. lateral to the midline. Through these openings a needle is inserted into the occipital horn of each lateral ventricle. The fluid is allowed to drain out and is replaced with air. It is better always to puncture both ventricles if possible and to bubble air through from one needle to the other. The roentgenograms are much better and much more easily interpreted if the ventricular system is as completely filled as possible. At any rate the air should never be injected under tension. This method of direct ventriculography has the advantage that an uncomplicated view of the ventricles is obtained. It has the disadvantage that it is difficult to fill the third and fourth ventricles in this way. When air does not enter the third ventricle one is never sure that it did not do so because the ventricle was occluded. But the method often furnishes much aid when the tumor lies within or around the cerebral hemispheres.

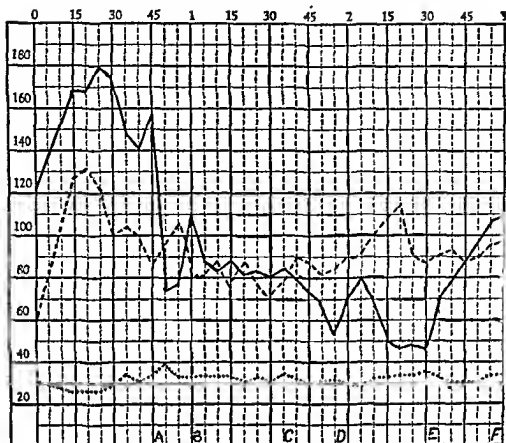
The methods of encephalography and ventriculography give evidence of the presence of a mass but none concerning its nature. Two methods have been proposed to aid in the pathological diagnosis. It has been suggested that a core of tissue be removed with a cylindrical sharp needle after trephination; this method risks a dangerous hemorrhage

and it is difficult to interpret the material removed. Useful information with less danger may be obtained by arteriography with thorotrast or other opaque medium. It is usually performed after exposing the artery surgically (346) but may be made by puncture through the skin (438).

So far we have been discussing diagnostic methods, but they are surgical methods and are really means of obtaining information necessary to planning the surgical intervention. We will suppose now that we believe a tumor to be present in the intracranial cavity, that we know where it is situated and possibly also its nature, and turn our attention to methods of removing it. Surgical asepsis must of course be observed, and with particular rigor, for the operation will be long and the cerebrospinal spaces an excellent place for bacteria to grow in. Just before the operation begins the patient's head is completely shaved and washed with soap and water. This should not be done the night before because scratches in the scalp are always made by the razor and in the time which intervenes between the shaving and the operation infection begins in these small wounds.

Preliminary medication is avoided at much as possible, particularly morphine. The respiratory center is almost always embarrassed in cases of intracranial tumor, especially in those of the posterior fossa. If ether is to be administered the intracranial tension will be still further increased and if now a respiratory depressant, such as morphine, is added respiratory paralysis may ensue. Narcotics are therefore avoided. If ether is to be given atropine may be used to lessen the secretion of mucus in the air-passages.

The choice of an anesthetic must now be made. Undoubtedly local infiltration of the scalp with novocaine is theoretically the ideal method of anesthesia (334). The cranium, meninges, and brain are practically insensitive except for the larger arterial trunks of the dura mater near the base. It suffices, therefore, to infiltrate the scalp along the line of incision with sometimes a little additional infiltration of the muscles. *The principal disadvantage of local anesthesia arises from the length of the operation.* The patient becomes very weary of lying in one position for a period of two, three, or even four hours, and usually becomes restless just when the surgeon wishes to make some particularly delicate manipulation within the brain. When the patient begins to complain the surgeon has a tendency to hurry and it is an accepted principle of intracranial surgery that *an intracranial operation should be done cautiously without regard for the time involved.* Intracranial operations



Time 2' 55" Resp. Pulse ---- Blood Pressure ———

FIG. 153. Anesthetist's chart of removal of a meningioma. A—elevation of bone flap causes a sharp fall of bloodpressure which rises (B) when the surgeon interrupts the operation and waits for a few minutes. Removal of the tumor (C) causes another fall of the bloodpressure which is raised temporarily (D) by an infusion of normal saline solution and permanently (E) by a transfusion of blood. The operation terminated at F.

under local anesthesia are also a terrific mental strain for most patients. If a secondary operation is necessary they beg to be put to sleep.

For the surgeon, general anesthesia is best. He feels much freer when the patient is asleep. The best general anesthetic is ether, especially for children. It is administered by a machine through tubes placed through the nares into the nasopharynx. Some anesthetists prefer to use an intratracheal cannula; it should be avoided in children since it is apt to provoke a laryngeal edema which may necessitate a tracheotomy. Ether may be given in this way for five, six, or even seven hours without

ill effects. The anesthetic is then in control of the anesthetist who can vary its depth at will. The anesthetist keeps a record (127) of the pulse-rate, respiratory rate, and of the systolic and diastolic bloodpressures, recording them every ten minutes or oftener if necessary, and warns the surgeon if alarming changes occur (Fig. 153). Colonic ether is not recommended because of the uncertainty of its absorption and of the impossibility of reversing the process once it is given. Some of the disadvantages of ether the cranial surgeon does not worry about, for example postoperative pneumonia is very rare and pulmonary embolus almost unheard of. It does, however, increase the intracranial tension and the capillary bleeding. When the intracranial tension is great one chooses rather to operate under local anesthesia if the patient is able and willing to cooperate. A general anesthetic is also dangerous when the patient has arteriosclerosis or cerebral lues.

Lately there has been a tendency to operate with various narcotics. Avertin by rectum, combined with local infiltration of the scalp, has been much used (160). Usually some ether must be added. It has a tendency to lower the bloodpressure and, therefore, the intracranial tension which may be advantageous in many situations. Usually, however, in any serious intracranial operation there is a struggle to keep the bloodpressure up and it seems foolish to handicap oneself at the outset. Sodium pentothal, given intravenously, is free from this defect and can be regulated continuously; it is now much in favor (176). Very satisfactory anesthesia can also be obtained with nitrous oxide given through a tracheal tube, but it is not recommended because of the frequency of cerebral anoxia (111).

The position in which the patient is to be placed is also important. Undoubtedly again on theoretical grounds there would be a great advantage to operate on all patients in the sitting position (334). In this way the intracranial pressure is reduced to a minimum and venous bleeding also. Both are great annoyances in intracranial surgery. But another annoyance which is much more serious is the tendency to syncope either from shock or hemorrhage. In this condition it is necessary to lower the head below the body. Operating-tables have been constructed which permit this but a satisfactory method of draping which will not be completely disarranged by this maneuver has yet to be devised. One will therefore compromise and keep the patient's head as high as possible, the actual position varying with the operation (343).

We come now to the opening of the head. In the older manuals of surgery many pages were devoted to elaborate methods of determining the exact location of various landmarks of the brain on the external surface of the head. The reason was that the surgeon at that time made a craniectomy with a rongeur and the bone removed could not be replaced. He was anxious, therefore, to open directly over the

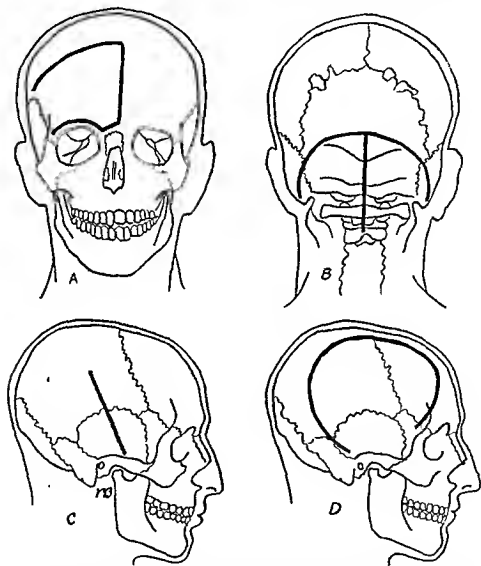


FIG. 154. Classical incisions for intracranial operations. A—approach to the hypophysis; B—approach to the cerebellum; C—incision for subtemporal decompression; D—approach to the cerebral hemispheres.

spot involved and to remove as little bone as possible. At the present time the necessity for a knowledge of such *minute craniocerebral topography is obsolete*. The surgeon makes a large osteoplastic craniotomy. Since the bone is replaced there is every advantage in making the opening as large as possible. The surgeon soon learns to know in a general way the situation of the lateral and central fissures, and of the ventricles, and this knowledge is sufficient.

The essential surgical approaches to the intracranial cavity are few (Fig. 154). The supratentorial region is almost universally approached by an osteoplastic procedure. This consists essentially of a horseshoe-shaped incision through the scalp, after which a series of holes are bored through the cranium along the line of incision in the scalp. The bone is cut through between the holes with a twisted wire (Gigli saw) which is passed from one hole to another between the cranium and dura mater and then sawed outward. The bone across the neck of the horseshoe is broken, which makes a flap of the bone and its attached scalp, with the intact scalp across the neck of the horseshoe as a hinge. This osteoplastic flap can be replaced and held in position by suturing the incision in the scalp.

The position of the osteoplastic flap may vary with the region to be explored. Usually in the temporal region the base of the flap is downward, in the frontal region the base is lateral and in the occipital region it is forward. These positions are chosen because the temporal bone is thin and breaks easily. But if one wishes to saw through the neck of the boneflap it may be placed in the occipital region for an occipital flap and in the frontal region for a frontal flap. Theoretically a better blood-supply would be secured through the occipital and supra-orbital arteries. Actually any area of the scalp is able to nourish a boneflap provided the neck be not narrower than five centimeters. One usually avoids the neighborhood of the venous sinuses which are liable to be torn when the bone is separated from the dura mater.

In the suboccipital region one usually makes a craniectomy. A curved incision (Fig. 154) is made in the scalp extending from the tip of one mastoid process across and above the external occipital protuberance to the tip of the opposite mastoid process. The scalp is then stripped downward below the superior nuchal line and another incision made through the suboccipital muscles, parallel to and just below their insertion. The muscles are then stripped downward to the foramen magnum and the bone removed with a rongeur. Usually the curved incision suffices, if

the extremities are carried down far enough, but if later it is found necessary a midline incision through the ligamentum nuchae may be made and extended downward to permit a laminectomy of the cervical vertebrae. A craniectomy may be made through the midline incision alone (205) but it is not usually advisable to do so because of lack of room for manipulation in the posterior fossa. A boneflap may also be turned down in the suboccipital region and is used to approach an acoustic neurinoma (38).

Once the dura mater is exposed it is palpated. If too tense there is danger in opening it because the soft brain-tissue may protrude through the opening and the cortex rupture. Different methods are available for lowering the intracranial tension. First an attempt is made to puncture a ventricle. If successful it may be possible to remove sufficient fluid to reduce the tension. It may be advisable to puncture the ventricle early in the operation if the bleeding is excessive or respiratory difficulties occur. This is particularly necessary in suboccipital operations where it is also usually easy because of the hydrocephalus. The ventricles may of course always be punctured through a trephine-opening. Fluid may be removed also through a lumbar puncture but this method is inconvenient and dangerous. If the ventricle cannot be tapped it is better to inject intravenously a hypertonic solution (504). And a 15 percent solution of sodium chloride (75 ccm.) should be chosen because in these circumstances one wishes a rapid and brutal effect. Within fifteen minutes the tension will be sufficiently reduced so that the dura mater may be safely opened, care being taken not to injure the pial bloodvessels beneath.

The exposed brain is inspected and palpated. Any change in color, contour, vascularity, or consistency is carefully noted. It is at this point that it is absolutely necessary to have an intimate knowledge of the structure, both normal and morbid, of the brain. *Anybody can open a head, for better or for worse, but only a neurologist can interpret what he finds, except in the most obvious circumstances.* And even the neurologist needs experience at the operating-table, for it is necessary to know the living brain. When the tumor is not visible on the surface the deeper regions must be explored. One may at times feel with the finger an increased resistance over the tumor or, in case it is cystic, a softer consistency. If further information is desired a blunt hollow needle is inserted into the brain in various directions and one judges by the resistance of the condition of the underlying structures. In this

way a cyst may be found and identified by the yellow clotting fluid which it usually contains. If one is still not satisfied an incision may be made in the brain and extended to the depth desired. Here again a knowledge of the structure of the brain is absolutely essential in order not to cause serious defects. The general surgeon is handicapped not only by a lack of knowledge but also by lack of respect for the brain-tissue. To the neurologist each cell and fiber is sacred. With full knowledge of the disastrous effects which may result from his actions, he handles the brain tenderly and with infinite precaution.

The tumor once located it may be dealt with in many ways, and *the procedure varies with each type of tumor*. The meningeal tumor over the vertex is the simplest to remove. It is attached to the dura mater, so that portion which is attached is carefully encircled and left adherent to the tumor. One then makes an incision in the pia-arachnoid surrounding the tumor, ligating all the pial arteries and veins which enter. The brain-tissue is now pushed away gradually from the surface of the growth. Usually the tension of the brain and the arterial pulsation aid in extruding the tumor from its bed; the process may be assisted by passing a few ligatures through the tumor and pulling gently with them. Since the meningeal tumor pushes the brain aside without invading it, the cavity which it leaves when removed is rapidly filled by the expanding brain. The defect in the dura mater need not be closed; a new mesothelial covering is rapidly formed.

This method of encircling a meningeal tumor and shelling it out of its bed often meets with difficulties. These tumors grow commonly along the great venous sinuses of the dura mater and the attempt to free them causes profuse venous bleeding from the sinuses, lacunae, and cerebral veins. In some cases the sinus can be ligated, but this is not easy because the dural sinuses are held open by the rigid dural septa. Moreover one dare not ligate the superior longitudinal sinus behind the entrance of the central veins for fear of a paraplegia and one must also avoid the central veins themselves (267). When a meningioma occurs over the base of the skull it may prove impossible to get around it for lack of room. Such a tumor must be removed piecemeal with a curette or better with an electrosurgical loop (134). The interior of the tumor is removed in this way; the capsule can then be dissected away from the brain.

The pituitary adenoma is approached under either frontal lobe, preferably the right in most cases, after a frontal or frontotemporal

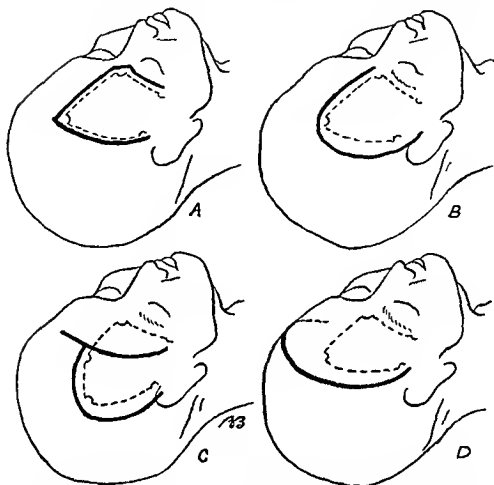


FIG. 155. Variations of the incision for tumor of the hypophysis. The incision in the bone is represented by the interrupted lines. A—the classical approach; B, C, D—variations.

boneflap (255) has been made (Fig. 155). The transphenoidal approach is now practically obsolete. One may go inside or outside the dura mater. The latter procedure, which is usually preferred, necessitates an incision in the dura mater along the sphenoidal ridge (207). The temporal intradural route to the chiasm should not be used except when the frontal extradural approach is impossible, because of the serious sequels which so often follow (see CASE IV, p. 90). The adenoma may be removed with a dull curette since it is usually quite soft. Sometimes it may even be sucked out. It is not advisable to make a radical removal. If one is unfortunate enough to remove the remnants of normal hypophysis, or to remove too much of an eosinophilic

adenoma, a hypopituitary syndrome may be precipitated for which at present we have no remedy. It suffices to remove as much as comes away readily so as to relieve the pressure on the optic chiasm. It should not be forgotten that branches of the *circulus arteriosus*, even the internal carotid arteries, may traverse the tumor.

The craniopharyngioma is approached in the same way as the adenoma or through a dilated lateral ventricle. Since it is often cystic the evacuation of the cyst *immediately reduces the tension*. The wall of the cyst is not firmly attached to the brain except at its base and may sometimes be pulled out between the legs of the optic chiasm and removed. One should never be content with evacuating the cyst. If a considerable portion of the wall is not removed the cyst will refill. After evacuation and removal of the thin wall the solid portion of the tumor is curetted away. Again a too vigorous curettage of the sella may be followed by severe hypopituitary symptoms.

An acoustic neurinoma is disclosed by retraction or amputation of a part of one cerebellar hemisphere or by transection of the lateral sinus and tentorium after elevation of the occipital lobe (38). The capsule of the tumor is then incised and the interior is removed with a curette. This is easy in those which have undergone extensive fatty degeneration. If the tumor is too bloody an electric loop must be used. In favorable cases the capsule may then be dissected away and removed, but it is often so firmly bound to the surrounding structures as to make this hazardous. When the capsule is removed the facial nerve may be removed with it and occasionally other nerves.

A pineal tumor is approached through a dilated lateral ventricle or between the cerebral hemispheres by transecting the splenium of the corpus callosum (149). A small tumor may then possibly be shelled out, but the successful removal of a tumor from this difficultly accessible situation, surrounded as it is by great venous sinuses, will always be largely a matter of luck. The chordoma is even more inaccessible.

In all the foregoing cases the problem is relatively simple and the operative procedure practically stereotyped. *The gliomas present more complicated problems, and the methods of different surgeons, even of those who operate routinely on such tumors, vary greatly.* It is in dealing with these tumors that the individuality of the surgeon and his knowledge of the structure of the brain and the behavior of its tumors is most apparent. I can do no more than to give my own present attitude toward this difficult problem. Gliomas infiltrate the

surrounding tissue; they are never encapsulated although sometimes fairly sharply circumscribed. It is then theoretically proper to remove them by cutting widely into the surrounding brain. But one cannot do this with impunity. It is always necessary to weigh the result for the patient. I am not one of those who would remove half of the brain without regard to the fact that I might leave the patient without his intellect or the means of making it effective.

The operative procedure will vary also with the type of glioma. When one is disclosed I make an immediate biopsy. If the tumor proves to be a medulloblastoma I am content to make a decompression, removing only enough to relieve the circulation of cerebrospinal fluid. Attempt to remove it completely is dangerous and futile. I have never known one to be successfully extirpated and I have witnessed numerous attempts by a master-surgeon. The tumor inevitably recurs in a few months. Just as long an interval of freedom from symptoms may be secured by decompression alone followed by roentgen-radiation. An astrocytoma I always attempt to remove. This is particularly easy when it is cystic. The evacuation of the cyst gives room for the manipulations necessary for the removal of the mural tumor. If it is successfully removed, cutting widely into the surrounding nontumorous tissue whenever possible, the patient will be permanently cured. If the mural tumor cannot be removed the cyst will sooner or later refill.

Any other type of glioma I attempt to remove only if it occupies the tip of an occipital lobe, of the right temporal lobe, or either frontal lobe. In all cases an amputation of the lobe is made, cutting widely into the normal tissue. And I hesitate before amputating a frontal lobe. This procedure is always followed by more or less alteration in character and defect of judgment (241). In a washerwoman *these results may be of little concern but when the patient is a professional or businessman, who must make decisions affecting many other people, these results may be disastrous.* And how often is even the amputation of a lobe rendered ineffectual by the extension of the tumor into the deeper structures or through the corpus callosum into the opposite hemisphere (339). I have never known a glioblastoma multiforme to be permanently cured even by removal of the greater part of a hemisphere.

If I could be sure of my diagnosis I would rarely operate on a glioblastoma multiforme. Unfortunately, unless arteriography proves to be adequate, one can never be certain. I have had the experience

of telling the husband that his wife had a malignant glioma because of the rapid course with repeated cerebral insults; at operation I found an easily removable meningeal tumor. Such experiences as these make one almost always explore. But when, as so often happens, one's worst fears are confirmed, a dilemma is presented which must be faced boldly. Gliomas which there is small chance to remove I like to interfere with as little as possible. Many gliomas seem to grow much faster after operative interference. This is especially true of the protoplasmic astrocytoma and the oligodendroglioma. It may be that these tumors gave symptoms of increased intracranial tension because they had already begun to undergo malignant transformation. At any rate it is a fact observed by many that symptoms of pressure may recur rapidly after operation for an indolent type of glioma with a long clinical history; at a secondary operation the histological type is radically changed (468). In such cases I am content to make a subtemporal decompression and replace the boneflap (120).

But sometimes when the intracranial tension has been great and it has been necessary to give intravenous hypertonic solutions in order to open the dura mater safely one is no longer able to replace the boneflap, even after a decompression. Removal of the bone will enable the scalp to be resutured over the exposed brain but I hesitate to do this because an unsightly hernia is sure to develop and the wound may even separate with the formation of a fungus cerebri. In order to replace the boneflap I have not hesitated to remove not only as much as possible of the tumor but also extensive sections of the normal brain, particularly of the occipital, frontal, or right temporal lobes, even of the right parietal region. One makes, in this way, a sort of internal decompression, thus giving the boneflap time to grow firmly into place before the intracranial tension again becomes high.

As diagnostic procedures have been perfected the old decompressive operation, by removal of bone under the temporal muscle (119), designed only to relieve tension, has become almost obsolete. Almost always an attempt is made to remove the tumor through an osteoplastic opening, and the exploration is transformed into a decompression only if the tumor proves to be inoperable.

In operating for intracranial tumor there are principally three complications to be feared—hemorrhage, shock, and respiratory paralysis.

Hemorrhage begins from the moment the first incision is made and continues often even after the last suture is tied. The utmost pre-

caution must be taken to insure complete hemostasis throughout the operation (138). An oozing which would be of no importance in an operation lasting fifteen minutes becomes dangerous during an operation of three hours. The bleeding from the scalp may largely be checked by pressing the scalp firmly against the cranium along the line of the incision; since the bloodvessels run in the subcutaneous tissue they will be occluded. The pressure is exerted before the incision is made and released only after the vessels have been secured. In this way little blood is lost from the scalp. The hemostats are not placed on the vessels directly but along the edge of the galea so that when they are reflected the galea is curled over the edge of the scalp and all the vessels effectually occluded. The diploic and emissary vessels of the cranium are stopped by pressing wax (Horsley's) into them. The venous bleeding from the surface of the dura mater is very difficult to stop. Some of the vessels may be thrombosed by pressing upon them a large pad of cotton wet with salt-solution at 39.5° to 42° but the most effective method is to press upon the bleeding spot a fragment of muscle. The hemostatic properties of muscular tissue, known to the ancient Egyptians, make it invaluable in intracranial surgery. Small pieces may be obtained from the temporal or suboccipital muscles, but larger masses are often employed from the patient's gastrocnemius muscle or from another patient in an adjoining room who is having an amputation of a leg, breast, or other part which contains an ample supply of muscle. Lately better hemostatic agents have been discovered. Fibrin foam (18) is difficult to obtain in peace-time but gelatin may be used as a vehicle for the hemostatic principle (318).

The bloodvessels in the pia mater and brain have such delicate walls, except for the larger arteries, that it is almost impossible to occlude them with a hemostat and ligate them. The vessel is almost always torn in the attempt. Smaller veins and capillaries may be induced to thrombose by irrigation with hot physiological salt-solution or by packing with cotton wet in the same solution. Larger veins may be thrombosed by holding on them a bit of muscle, but when they are numerous it is better to use small V-shaped bits of silver which are clamped and left in place (138). Arteries are controlled with the same silver clips. Lately there has been a tendency to check the venous bleeding by charting the vessel and surrounding tissue with an electric current. *This method is not advisable.* It kills tissue, delays healing and increases the liability to infection. There is a severe meningeal reaction

to the absorption of dead material which does not always remain sterile. Especially near the brainstem the use of the electric cautery is hazardous (313). As the charred tissue is absorbed severe secondary hemorrhage sometimes occurs. The delicacy of the cerebral tissue makes it inadvisable to keep the operative field free of blood by the usual method of sponging with gauze. Irrigation with warm saline solution not only keeps the field clean but tends to check bleeding. The excess which does not run away is removed with a suction-apparatus. Sponging may be done gently with soft pledgets of cotton wet with saline solution.

If these methods do not suffice and enough blood is lost so that the bloodpressure falls off alarmingly it may be raised again by an infusion of physiological salt-solution. It is best given by inserting a cannula into a superficial vein near the ankle; the flow of salt-solution from a container may be regulated at will. The effect can be prolonged by using a solution of acacia (2) but I prefer to make a transfusion of blood if necessary. The blood is obtained from a suitably matched donor, filtered and poured into the same container from which the salt-solution was given. I have administered in this way during the removal of a hemangiomatous meningeal tumor more than 1500 ccm. of blood without any reaction. Filters for the blood have been recently perfected (360).

At times during an intracranial operation the bloodpressure drops suddenly, the pulse becomes rapid and feeble, the respirations shallow, and the skin cold and clammy. These evidences of *shock* follow commonly a sudden smart bleeding, the breaking up of a boneflap or the shelling out of a large tumor (cf. Fig. 153). If the bleeding is arrested, the head of the table should be immediately lowered and all manipulations suspended. Within ten or fifteen minutes, if there has not been too severe a hemorrhage or if the shock has been due to other cause, the bloodpressure will rise and the operation may proceed. The surgeon learns to judge when enough blood has been lost to necessitate a transfusion and when the symptoms are due to other causes.

Respiratory paralysis is usually due to pressure upon the central respiratory mechanism in the bulb. This pressure must be relieved. Sometimes it suffices to puncture the lateral ventricle. When this is not possible and the tumor is supratentorial an intravenous injection of hypertonic saline solution may improve the condition. When the tumor is in the posterior fossa and the tension is not reduced by puncture of the lateral ventricle it is necessary to open the suboccipital

region as rapidly as possible and empty the posterior cistern. In some cases a laminectomy of the first and second cervical vertebrae must be made. If respiration ceases in the meantime artificial respiration is resorted to while the above mentioned measures are being carried out.

When all manipulation within the dural cavity has been completed and all bleeding carefully checked it is customary to close the dura mater over the cerebrum except where it is desired to leave a decompression. Over the cerebellum the dura mater is usually left open. I believe, however, that when an astrocytoma has been removed and no recurrence of the tumor is expected it is best to close carefully the dura mater. In this way perhaps one may avoid the formation of subarachnoid cysts in this region which sometimes are more difficult to eradicate than the original tumor. Over the cerebrum the external surface of the dura mater and the internal surface of the boneflap must be cautiously scrutinized and all venous oozing stopped. The boneflap is then replaced and the closure of the wound is ready to begin. No drains are inserted, except under extraordinary circumstances.

Careful closure of a wound which has opened the subarachnoid space is very important, otherwise a fistula of cerebrospinal fluid readily forms along which infection enters the meninges. This was formerly one of the most dreaded of the complications of intracranial surgery. The muscles may be closed with catgut but the subcutaneous tissue and skin must be approximated as exactly as possible with numerous interrupted sutures of fine silk. A separate layer of sutures must be placed in the galea aponeurotica. If the wound is not perfectly and firmly closed, and any tension is exerted subsequently from within, it may separate and a distressing fungus cerebri form.

The patient should not be put to bed until the bloodpressure and respiration are satisfactory. If there is any doubt he is left lying on the operating table until completely recovered from the anesthetic. This is especially important after operations in the posterior fossa. Such patients sometimes cease breathing abruptly when transferred to bed. *The patient should always be put to bed in an almost sitting posture* and every attempt should be made to improve his condition so that this posture is possible. It is the most important beginning of his postoperative care. The formation of an intracranial blood-clot from continued venous bleeding is the most feared postoperative complication at the present time. Since the intracranial venous pressure

is at a minimum when the patient is in an upright position he should be left for the first two or three days as nearly as possible in this position. In this way the danger of postoperative bleeding is greatly reduced. Such a blood-clot may form within the dura mater but is usually situated between the dura mater and the bone. The symptoms produced are those of *acutely increasing intracranial tension* and the patient becomes stuporous and finally comatose, the pulse is slow, the bloodpressure rises, the respiration slows, and finally periods of apnea occur (126). The pupil on the side of the hemorrhage is dilated (395). Sometimes there is no change in the bloodpressure and, if ether has been given, the patient may never recover consciousness. Since the effect on pulse, bloodpressure, and pupil may be transitory, a nurse is always in constant attendance on a patient for two days following a craniotomy. She records the pulse, bloodpressure, and pupillary diameters every half hour during the day and every hour at night. Another sign of increasing intracranial tension, especially if there is a clot between the dura mater and the cranium, is elevation of the boneflap. If the bleeding is within, the dura mater prevents much pressure on the boneflap.

Similar symptoms may sometimes be produced by acute cerebral edema following removal of a tumor. If suspected an intravenous injection of a hypertonic solution of glucose may improve the condition of the patient. In case of doubt it is always advisable to reopen the wound.

Another dreaded postoperative complication is *hyperthermia*, which develops usually after operations around the brainstem, from the hypothalamus backward. The temperature rises acutely, perspiration ceases, the pulse is usually rapid, and consciousness arrested. The patient's clothes should be completely removed and constant sponging with alcohol or iced water resorted to. If the rise of temperature does not cease ice-packs should be used. Even this heroic measure is sometimes of no avail; the temperature continues to rise and death soon occurs. The temperature should be carefully watched and as soon as there is a definite trend downward less strenuous measures should be substituted because afterward the temperature may fall to a very subnormal level and necessitate the application of heat.

Respiratory difficulties continue sometimes after extensive operations in the posterior fossa. The patient should be kept with the face down as much as possible and the position of the neck changed as

little as possible. Artificial respiration may be necessary. Improvement may follow puncture of the lateral cerebral ventricle.

Infection is rare in intracranial surgery. If one occurs we are now much better prepared with remedies (382).

Other less common and dangerous complications are mental aberrations, headache, vomiting and difficulty of swallowing. They will be treated as reason counsels. Vomiting is particularly annoying because it increases intracranial tension and may start bleeding.

The cutaneous sutures are removed in forty-eight hours, earlier over exposed parts such as the forehead. This helps to prevent infections which are exceedingly rare in cranial surgery. If a fistula of cerebrospinal fluid develops, packs wet with 70 percent alcohol are kept over the opening and it is closed as soon as possible. Drains are never used except in the rare case in which it has proved impossible to check the venous oozing. In my experience they drain cerebrospinal fluid but rarely blood.

A better conception of the problems which arise postoperatively may be obtained from the study of a few concrete examples. The matter is of sufficient importance to justify the time. I have had a surgeon tell me with a surprised expression on his face that he made his ventriculogram according to all the rules and the patient seemed all right that evening but when he returned to the hospital in the morning the patient was dead!

The first patient (CASE LXV) is a young man of twenty-seven who was operated on for cerebral tumor. A large ragged cavity was found in a tumor which occupied the greater part of the left parietal region. In its wall there was tumor everywhere. A subtemporal decompression was made. The wound was dry. There was left a large cavity caused by evacuation of the cyst. At the end of the operation the bloodpressure was 100/42 and he seemed to be in very good condition. Because of the lowered intracranial tension and lack of bleeding he was placed flat in bed. At 8:00 A.M. the following morning his temperature was 39.2° and the pulse rate 108. His bloodpressure was 124/64. There was a complete right hemiparesis. He was quiet all that day and his condition changed little except that his temperature gradually subsided. The following day he seemed better, answered when spoken to but with evident dysarthria. At 8:00 A.M. of the third day his temperature was 37°, pulse rate 64, and bloodpressure 104/60. He slept most of the time and ate well. At 8:00 A.M. of the fourth

day temperature was 37.6°, pulse 72, and bloodpressure 100/64. He seemed very well. During the fifth day his condition was unchanged but during the sixth day he became stuporous and his pulse varied from 56 to 100. We had by this time ceased to take his bloodpressure. The decompression, however, was not bulging and the boneflap was firmly in place. At 8:00 A.M. of the seventh day his temperature was 39.6°, the pulse 134. He was comatose and breathing stertorously. The boneflap was elevated and the decompression tense. Over 100 ccm. of mixed blood and cerebrospinal fluid were aspirated with a lumbar-puncture needle through a trephine-opening. This did not improve his condition. His temperature remained from 39.2° to 40.5°, the pulse around 150, and he never regained consciousness. Symptoms of pneumonia developed. He died on the morning of the tenth day. Necropsy disclosed a large ragged cavity (5 x 5 cm. in diameter, in a glioma of the left parietal region. It was filled with bloody fluid. Between the dura mater and the cranium was a small amount of clotted blood. There was also a bilateral suppurative bronchitis with pulmonary edema and bronchopneumonia.

There must have been some continued bleeding into the cystic cavity but this is not enough to account for the condition. The material evacuated was mostly cerebrospinal fluid. It is probable that the ventricle had been opened by the collapse of the brain and this had been blocked suddenly by blood-clot or debris. We were warned of the seriousness of his condition by the stupor and the irregularity of his pulse and should have watched him more closely. After the puncture he could no longer adjust his neural apparatus and probably was already developing a bronchopneumonia.

The mere collapse of the brain following evacuation of a large cyst is sometimes enough to precipitate grave symptoms. A woman (CASE XXVI) of forty-five was operated on for a frontal tumor and an enormous cyst evacuated from the right frontal lobe. There was obviously glioma in the wall of the cavity but we made no attempt to remove it, except a small fragment for verification. She did not recover consciousness for three days. The temperature was kept under 40° by sponging; the pulse was 120-140. The bloodpressure rose from 129/100 to 168/100. But knowing that there was no bleeding when the wound was closed and because there was no elevation of the boneflap we did not open the wound. She had been constantly in the sitting posture. Finally on the third day the temperature and pulse

rate slowly descended, the bloodpressure subsided to 130/96 and she recovered consciousness.

It is well to remember that these things may happen when a large cavity in the brain has been evacuated. A police-officer (CASE LXVI) who had epilepsy following a fall from a motorcycle was found to have a large subarachnoidal cavity in the left frontal region. An osteoplastic operation was performed with local anesthesia. The cystic cavity was enormous. It was evacuated and adhesions were loosened which opened it into the surrounding subarachnoidal spaces. During the operation the patient had an epileptic attack and slept soundly afterward. His pulse and bloodpressure had changed not at all and there was no bleeding. However, he never regained consciousness. His temperature steadily rose until on the morning of the third day he died with a temperature of 40.5° . His pulserate was very irregular. At one moment it would beat at a rate of 45, full and bounding; an instant later the rate would be 130-140 and feeble. An electrocardiogram showed that in the slow periods there were many cycles without evidence of auricular activity, others with a P-R interval of 0.10 to 0.14 sec. and still others showing retrograde waves. This effect was probably due to central stimulation of the vagus since it disappeared after administration of atropine. The heart then beat at a regular rate of 128 per minute, P-R interval 0.12 sec., sinus rhythm and QRS complex 0.06 sec. During all this time the boneflap was firmly in place although the bloodpressure rose steadily from 112/72 to 150/68 on the morning of the second day. Necropsy showed that there had been no intracranial bleeding. The symptoms were probably due to collapse of the brain and acute disturbance of the central mechanisms of the hypothalamic region.

Symptoms due to acute disturbance of the hypothalamic region often follow operations for tumor of the third ventricle. A young man (CASE XLVIII) of twenty-two with obesity, polyuria, genital dystrophy, and other symptoms due to a calcified tumor in the suprasellar region was operated on for a supposed suprasellar cyst but a solid tumor was found which could not be removed. Only a fragment was removed for verification and there was no bleeding. But the patient did not regain consciousness. The temperature rose to 39° by 3 P.M. of the day of operation. With sponging the temperature was maintained constant but the pulserate began to fall. It was 128 at 7:00 P.M., 112 at 8:00 P.M., 92 at 9:00 P.M., and 72 at 11:00 P.M. Meanwhile the blood-

pressure rose. It was 132 at 7:00 P.M. and by 11:00 P.M. it was 160. At 2:00 A.M. the pulse rate was 88 and the blood pressure 186. The bone flap was in place. The lateral cerebral ventricle was punctured. Colorless fluid was obtained under no pressure, but from that time the blood pressure dropped irregularly to 112-118, the pulse rate rose to 150-160 and the temperature to 40.5°. In this condition he died at noon on the day following operation. During all this time there was absolutely no sweating; the face was flushed but the body was pale. He seemed to be sleeping peacefully most of the time but had occasional periods of hyperpnea and occasionally twitching of the left arm. The temperature was not affected even by packing in ice.

It is obvious from the foregoing examples that the classical dissociation of pulse and blood pressure must be interpreted in the light of the other symptoms and is not pathognomonic of increased intracranial tension. I am not sorry that I cannot show you an example of postoperative intracranial hemorrhage. Since I am careful of hemostasis and put my patients to bed sitting up I have had only one such complication in three years, and that followed the use of the electric scalpel. I can, however, show you an example of postoperative edema.

This man (CASE LXVIII) of forty-eight years had a metastatic carcinomatous nodule about 4 cm. in diameter in the right central region removed. There were no symptoms of intracranial hypertension before operation and only slight weakness of the left arm and face. The operation was made with local anesthesia. There was practically no bleeding. He returned to his room with pulse rate of 120, blood pressure 120. The left arm was completely paralyzed, but he was conscious. The next morning he complained of pain in the head. The pulse rate was 100 and the blood pressure had risen to 148. His temperature was 38.4°. At 7:30 P.M. the temperature was still 38.4°, the pulse rate 118, and the blood pressure 122. Because he had been unable to swallow without choking a hypodermoclysis was ordered. By midnight the pulse rate was 84 and the blood pressure had risen to 164. He was very restless and complained of pain in the head. In the morning he was better again with a pulse rate of 100, blood pressure 148, and temperature 38.4°. During this first day he was again unable to swallow fluids so towards evening another hyperdermoclysis was given. By midnight he was semi-comatose, the pulse rate dropped to 64, and the blood pressure rose to 164. He then gradually improved and by 8 A.M. of the second postoperative day the temperature was 38.4°, the pulse

rate 88, and the bloodpressure 150. He remained, however, stuporous, yawned continuously, and complained of violent pain in the head. The conditions varied little during this day. At 8:00 P.M. the dressing was changed. The decompression was only slightly tense and the bone-flap was only slightly elevated. We had remarked that any attempt to give him fluids made him much worse. At 9:00 P.M., 50 ccm. of 50 percent glucose were given intravenously. His condition improved in a short time. The following morning he was much better, temperature 37.5° , pulserate 90, and bloodpressure 130. From that time his fluids were restricted and he improved rapidly. His pulserate still varied markedly from 50 to 100 but the bloodpressure never rose again and he did not again fall into a stupor. We were aided in this case in properly interpreting the symptoms by the observation that administration of fluids increased the symptoms and by the knowledge that carcinomatous metastases are apt to cause massive edema of the cerebrum.

These examples will suffice to show that the problems of intracranial surgery do not cease when the patient is put back to bed. Constant vigilance is necessary for several days, demanding a trained nurse in constant attendance.

The immediate postoperative period over, we are confronted with the care of those patients whose tumors have not been removed or only partially removed. What can be done for them? There is no medical treatment except for the relief of symptoms, such as headache, with various analgesic drugs. Intracranial hypertension may be reduced by administration of magnesium sulphate by mouth but the effect is quite transitory and it is useful only as a temporizing measure while an operation is in preparation. The only hope is in radium and roentgen-radiations. Their effect on some intracranial tumors is startling but they should rarely be used before operation. I advise their preoperative use only in cases of pituitary adenoma and intracranial angioma and then only with infinite precaution. Acute cerebral edema may follow radiation and cause death unless a decompression has previously been made. Since a pathological diagnosis is not always possible before operation much time may be lost in radiating a type of tumor which is not improved by such treatment. Moreover the use of radium (412) is not advised. It cannot be controlled as well as the roentgen-rays, is more difficult to apply, and more expensive. Roentgen-radiation is just as effective as radium (52).

Radiation therefore, except in rare instances, is a part of the postoperative treatment of intracranial tumors. *It is most effective in certain types of glioma, notably the medulloblastoma.* Glioblastoma multiforme is often sensitive to radiation but severe hemorrhages into the tumor are apt to occur. The other types of glioma are less certainly affected by this treatment but I radiate them all (with the exception of the fibrillary astrocytomas) because it is the only hope and perhaps one may discourage in this way the tendency of some of them to increase in malignancy. The intensity and persistency of radiation varies in every case and no general rules can be made at present. In my experience the meningiomas, neurinomas, and craniopharyngiomas are not affected by the roentgen-rays. Pituitary adenomas and angiomas are often very much improved by this treatment. The physician should not forget that *excessive radiation may result later in degenerative changes of the cranium (97) or brain (361, 479).*

When the symptoms recur the question of a secondary operation arises. Again no general rules can be made except in the case of an astrocytoma. It should always be reoperated on because a recurrence almost always means that the entire tumor was not removed at the first operation and that the cyst has refilled. Often at a second operation the position of the tumor has shifted so that it is more accessible.

With operations conducted in the manner I have described what are the results? We will take statistics recently published (182) and analyze them, realizing that statistics need always to be interpreted.

Mortality Rate at the Peter Bent Brigham Hospital Between May 1, 1928, and Jan. 1, 1929

Diagnosis of Tumors	Number of Patients	Patients Operated On	Operations	Postoperative Deaths	Mortality of Patients, percent	Operative Mortality, percent
Verified	128	111	144	16	14.4	11.1
Unverified	42	16	20	0	0.0	0.0
Total	170	127	164	16	12.6	9.7

In explanation of this table it should be stated that a tumor is classified as verified when it has been examined microscopically, either after operation or necropsy, and as unverified when it has not been examined microscopically but the surgeon feels sure from seeing or feeling or otherwise that a tumor actually exists. A death is called postoperative when it occurs in the hospital before discharge of the

patient no matter how long after the operation. The mortality of the patients exceeds the operative mortality because many patients have more than one operation.

It is obvious that this particular table means little. To have meaningful statistics must deal with comparable units. This table includes all sorts of intracranial tumors. The operations moreover are not all comparable, but vary from a simple craniectomy, through evacuation of cysts, to partial and sometimes complete removal of tumors. The only common factor in these statistics is the fact that the cranium was opened and *they prove admirably that craniotomies in the presence of intracranial tumors may be made with a mortality not much greater than 10 percent.*

Mortality Percentages in Cases of Verified Intracranial Tumor to Jan. 1, 1929

Diagnosis	Number of Patients	Patients Operated On	Operations	Postoperative Deaths	Operative Mortality, percent
Gliomas (varia)	690	624	946	184	19.4
Adenomas (chiefly pituitary) . .	302	295	337	21	6.2
Meningiomas	206	199	368	42	11.4
Neurinomas (acoustic).	141	133	181	23	12.7
Congenital tumors (chiefly cranio-pharyngeal)	99	94	145	18	12.4
Metastatic and invasive tumors. . .	64	50	62	13	20.9
Granulomatous tumors.	46	37	45	13	28.8
Bloodvessel tumors	29	27	39	3	7.6
Papillomas	11	9	19	3	15.7
Miscellaneous	54	45	68	8	11.7
Total	1,642	1,513	2,210	328	14.8

We will take now more detailed statistics from the same source (cf. table above). The same criticism may be made covering the operative procedure. But the following table shows clearly the influence on the mortality of the type of tumor present. And even these statistics are not sufficiently detailed. We have already learned how heterogeneous is the group of gliomas and that they cannot satisfactorily be treated as a whole. To take as an example the gliomas of the cerebellum in children, of the two principal varieties the medulloblastoma will have a very high mortality, around 30-35 percent, whereas the mortality for astrocytoma will be certainly below 10 percent. The statistics of mortality prove again, what I have always maintained, that intracranial tumors cannot be profitably discussed as a whole.

The mortality-rate of a surgeon may be a measure of his increasing knowledge and experience, but it may also indicate his timidity or his

temerity. One surgeon who never does more than a decompression in the presence of a glioma (430) will necessarily have a much lower mortality than another who attempts to remove the entire hemisphere containing the tumor (150). The accuracy of preoperative diagnosis has also a great influence on the mortality. The stage of the disease at which operation is performed and many other conditions also have their influence.

And these statistics give us no information concerning the outcome of operation on those patients who survive. How many patients were returned to society as self-supporting economic units and for how long? And in how many cases was the tumor extirpated and the patient permanently cured? And if permanently with what defects? Concerning these matters few reports are available (93, 480). *We must study each type of tumor separately to satisfy ourselves concerning these questions.*

We will begin with a relatively simple and uniform type of tumor, the acoustic neurinoma. After a long series of disastrous attempts radically to extirpate this tumor, which almost invariably comes to the surgeon at an advanced stage of its development, the method of intracapsular enucleation was adopted (122). The capsule is split and the interior of the tumor removed with a curette or electric loop until the capsule can be collapsed. Admittedly incomplete, this method gives relief with a minimum of risk. The immediate mortality is 11-12 percent. The symptoms of intracranial hypertension are relieved for a variable period up to five or six years. When they recur a similar procedure may be repeated. An attempt to remove the capsule of the tumor increases the mortality from hemorrhage or other complications and the morbidity from damage to nervous structures in the neighborhood, yet complete extirpations are being made more frequently (278, 364). Few patients are able afterwards to work.

A somewhat similar procedure is adopted for pituitary adenomas. The immediate operative mortality is from 6 to 10 percent. Although only a partial extirpation is made, roentgen-radiation effectively holds the remaining remnant in check so that the patient's eyesight is saved. Even severely damaged vision may be largely regained. The greatest remaining defect is the hypopituitary syndrome which seriously affects the patient's efficiency and against which we have at present no remedy. Most of these patients continue to work at lower efficiency.

The craniopharyngioma is not so favorable for treatment. The immediate mortality will always be great from acute nervous symptoms

produced by collapse of the hypothalamic and thalamic regions of the brain. Perhaps a mortality of 20-25 percent is the best that can be hoped for at present (477). This tumor is rarely completely removed. Evacuation of the cyst is not sufficient, but removal of as much as possible of the wall of the cyst is necessary to prevent the cyst from reforming. Too radical removal of the intrasellar portion of the tumor must be avoided because a severe hypopituitary cachexia may follow. Diabetes insipidus is a common sequel of operations on these tumors. Most of the patients are children and I know of no study of the end-results in these cases.

The meningiomas are the most favorable of all intracranial tumors for operative treatment. They can usually be removed completely although sometimes portions must be left along the great venous sinuses. The immediate mortality is rather high, from 10 percent upward in the hands of different surgeons, because of their vascularity. The resultant neurological defects depend on the size and site of the tumor but the great majority of these patients are permanently restored to health and economic efficiency. It is in the removal of these tumors that the electric scalpel finds its greatest usefulness. It can be used to remove the interior of meningiomas thus reducing their size and making the dissection of the remainder much easier (134).

Of the rarer tumors the hemaangiomas of cerebellar cysts may be removed and the patients permanently cured. Racemose angiomas had best be left alone surgically but roentgen-radiation may cause marked improvement. The pearly tumor is easily and permanently removed. The pinealoma will rarely be completely removed, the papilloma may more frequently be.

We come now to the vast group of the gliomas which I have deliberately left to the last. *It is difficult to say anything intelligent concerning them* except that an attempt should always be made to remove an astrocytoma; when successful the patient is permanently cured. Concerning the rest of them it will be a long time before it is possible to compare one surgeon's results with another's and any talk of "scores" is useless. The gliomas vary so much in site, structure, and stage of evolution, and the operative procedures adopted are so different, that statistics are meaningless. Gliomas of the optic chiasm, brainstem, and corpus callosum are inoperable, whatever their type. Roentgen-radiation may improve them but a fatal outcome is inevitable. I have never known a medulloblastoma or glioblastoma multiforme which did not recur

no matter how radical the attempt at extirpation. It is much the same for the other types, with the exception of the astrocytomas which make the one bright spot in the otherwise gloomy outlook, although the other types may survive for a variable time after operation. We should not forget also that the symptoms are often aggravated after craniotomy when a glioma is disclosed, especially in the case of the glioblastoma multiforme.

However dissatisfied we may be with the results of our surgical treatment it does not mean that we must abandon our efforts. On the contrary, they must be redoubled. What is the alternative if the tumor cannot be removed? Blindness and a horrible, painful, sometimes lingering, but inevitable death. If we could only make a certain pathological diagnosis before operation many futile operations would be avoided, but even after years of experience with intracranial tumors an occurrence such as the following makes one realize that in the present state of our ignorance an exploratory operation is almost invariably advisable.

A woman (CASE LXIX) of fifty-nine, previously healthy, had an attack of dizziness while at church. Her jaw dropped and for a time saliva drooled from the left corner of her mouth. She had headaches for a few days and was then well for about five months when a similar attack occurred, followed by a severe headache. She was carefully examined at this time and nothing found except a slightly elevated bloodpressure and a left lower facial paresis; the optic discs were normal. A month later she had a period in which she was nauseated and vomited frequently. After this she improved but was worried and emotional and her memory for recent events failed. Her voice was hoarse and she had difficulty in swallowing. This state continued for three months; she then began to complain of severe headaches, became suddenly stuporous one day and was brought to the hospital.

Until the final episode she had been thought to be suffering from cerebral arteriosclerosis. On admission to the hospital she was stuporous. There was an obvious left lower facial weakness and the optic discs were choked about 1.5 diopters. The bloodpressure was 160. Roentgenogram of the head was normal. The husband was told that in all probability there was a malignant infiltrating glioma in the right cerebral hemisphere and that little could be accomplished except to make a decompression. At operation a meningioma was found in the lateral fissure and easily removed. There was in addition an area of softening which involved the lower extremity of the anterior central

gyrus and the posterior extremity of the middle and inferior frontal gyri. It had doubtless been produced by occlusion of the prerolandic artery by the pressure of the tumor. The patient recovered completely except for the facial weakness.

In addition to this *uncertainty of diagnosis, which makes an exploratory operation almost always advisable*, there is another legitimate reason for operation. Much suffering can be avoided by decompressive procedures, and these are also advisable as preliminary to roentgen-radiation. But the hope of the future seems to lie in the direction of increasing our knowledge and diagnostic acumen so that we can foretell before operation, in an increasingly larger percentage of cases, the nature of the tumor to be attacked as well as its location. With the record of the last fifty years before us no one should claim that this goal is impossible of attainment. Recently arteriography has come to our aid. At present much of our effort is blind; it must be made less so.

Finally *in evaluating the results of operation for gliomas we must remember that we are operating for the "cancer" of the brain. The results are about as good as for cancer elsewhere in the body and the operative procedures little more desperate.* The reasons for persisting in spite of repeated failures are the same in cancer of the stomach and cancer of the brain. If the surgeon cannot remove a cancer of the stomach he relieves the symptoms by a gastroenterostomy. If the surgeon cannot remove a glioblastoma of the brain he also relieves the symptoms by a decompression. In 1898 Ferrier wrote: "The treatment of intracranial tumors forms a rather melancholy chapter in therapeutics." It is much less sad than then, yet in spite of remarkable progress in the sixty years which have elapsed since Godlee's epoch-making operation the surgical treatment of intracranial tumors is still a precarious, backbreaking, and heartrending business to be undertaken only by those who have especially prepared themselves for it.

INTRACRANIAL TUMORS

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LEGENDS FOR PLATES

Some of the roentgen photographs have been retouched. The short white rods in some of the photographs are silver clips left by the surgeon. The arteriograms were made by percutaneous puncture into the common carotid artery, so that branches of the external carotid arteries are also visible.

PLATE I

Acoustic neurinoma. From CASE II. Roentgenograms of the petrous pyramids. Right pyramid above; meatus dilated by tumor. Left pyramid below; meatus normal.

PLATE II

Adenoma of the hypophysis. Above, from CASE III, chromophobe adenoma; below, acromegaly. Sella turcica ballooned in both photographs

PLATE III

Above, *Medulloblastoma.* Separation of the cranial sutures. Below, from CASE VIII, *Craniopharyngioma.* The sella turcica is enlarged; there is a calcification above the sella. The cyst has been filled with air by puncture through the dilated suture.

PLATE IV

Meningioma of the sphenoidal ridge. Above, lateral view, below, antero-posterior view. The sphenoidal wing has been provoked to dense proliferation of bone by the invasion of the tumor.

PLATE V

Meningioma. Above, proliferation of bone provoked by invasion of the cranium by a parasagittal tumor (From Cushing and Eisenhardt). Below, arteriogram.

PLATE VI

Oligodendrogliomas. Calcification in the tumors. Above, from CASE XXVII; below, unusually dense calcification

PLATE VII

Polar spongioblastoma. Roentgenograms of the optic foramina. Above, from CASE XXXVI; the left foramen is enlarged. Below, from a case in which both foramina are enlarged.

PLATE VIII

Above, shift of the calcified pineal body to the left. Below, *Pinealoma*. Occlusion of the posterior part of the third ventricle by pineal tumor. Ventriculogram.

PLATE IX

Carcinoma of the lung. Roentgenograms of the chest. Above, large mass in the right hilum. Below, from CASE XLV, atelectasis of the lower right lobe.

PLATE X

Ventriculogram, Hydrocephalus. Above, anteroposterior view; below, lateral view.

PLATE XI

Ventriculogram, Tumor in the right frontal lobe. The ventricular system is displaced to the left and the anterior part of the right ventricle is displaced downward and partially occluded. Above, anteroposterior view; below, left lateral view.

PLATE XII

Arteriograms. Above, *Glioblastoma*. Note the tangle of vessels in the rostrum of the corpus callosum. Below, *Astrocytoma*. Note the displacement of the middle cerebral artery upward.

PLATE XIII

Above, *Sturge-Weber Disease*; calcification in walls of occipital sulci. Below, *Angioma*. Arteriogram.

PLATE XIV

Angioma. Above, venogram; below, arteriogram.

PLATE XV

Arteriograms. Above, normal except that the posterior cerebral artery comes off the internal carotid. Below, an *Aneurysm* of the internal carotid artery.

PLATE XVI

Metastatic Carcinoma. Above, single metastasis in the frontal bone; below, erosion of the base of the skull by a nasopharyngeal cancer.

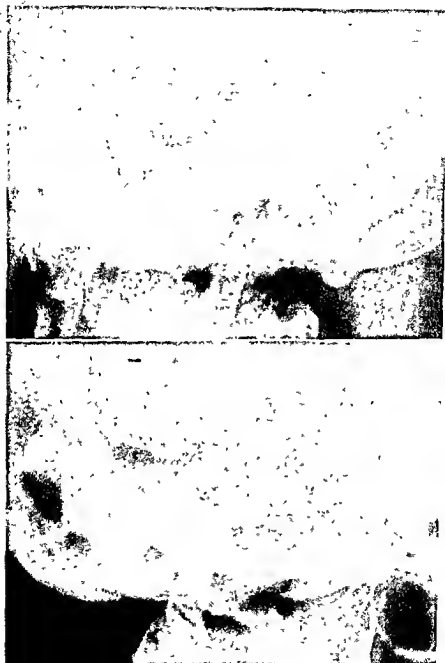


PLATE I

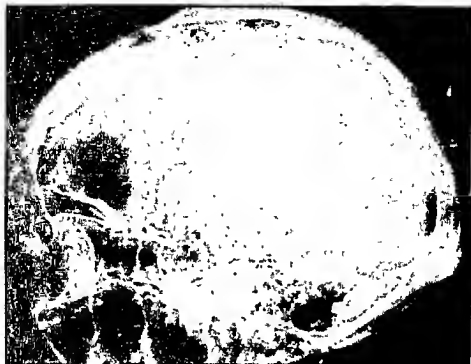


PLATE II



PLATE III



PLATE IV

1924



1925



PLATE V



PLATE VI



PLATE VII



PLATE VIII



PLATE IX



PLATE X

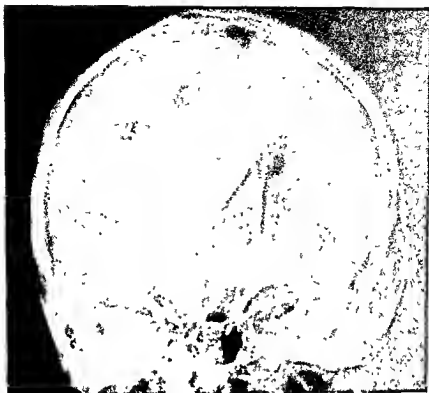


PLATE XI

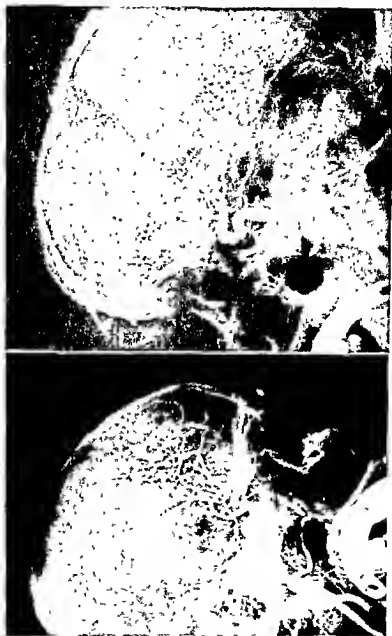


PLATE XII

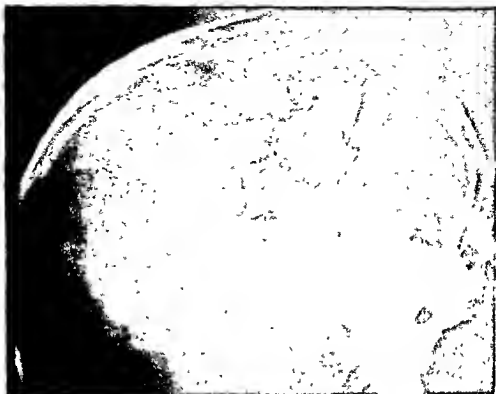


PLATE XIII

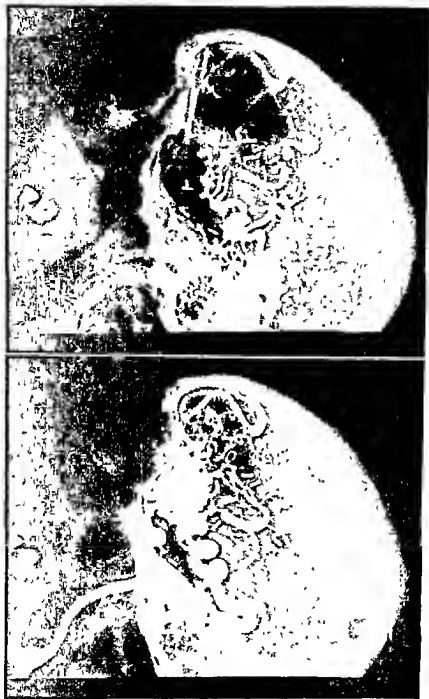


PLATE XIV

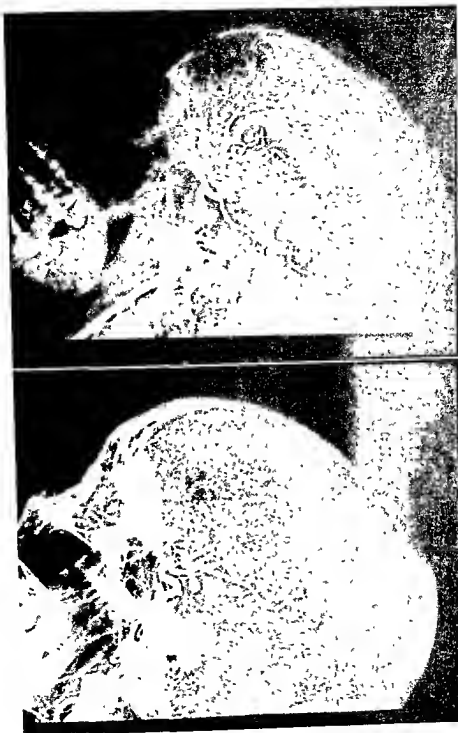


PLATE XV



PLATE XVI

THIS BOOK

INTRACRANIAL TUMORS

By PERCIVAL BAILEY

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